

10/762,730

STOR- structure Search

1.24.05

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ANSWER 1 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:872784 CAPLUS

DOCUMENT NUMBER: 141:366131

TITLE: A preparation of 2-azabicyclo[3.3.1]nonane derivatives useful as opioid receptor antagonists

INVENTOR(S): Coe, Jotham Wadsworth; McHardy, Stanton Furst

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: PCT Int. Appl., 45 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004089909	A1	20041021	WO 2004-IB1237	20040402
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.:

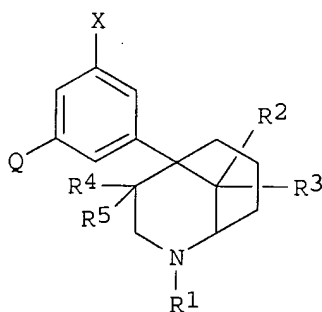
US 2003-462605P

P 20030414

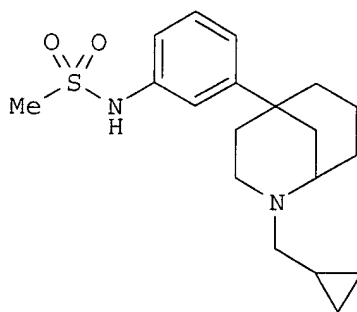
OTHER SOURCE(S):

MARPAT 141:366131

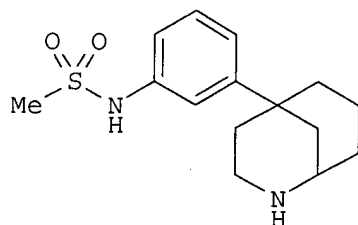
GI



I



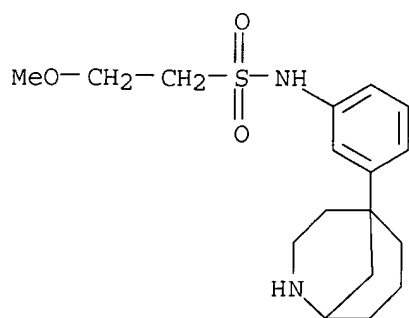
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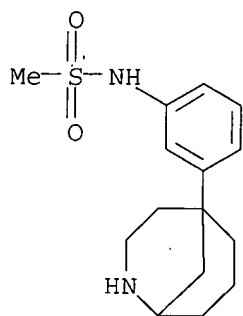
III

AB The invention relates to a preparation of 2-azabicyclo[3.3.1]nonane derivs. of

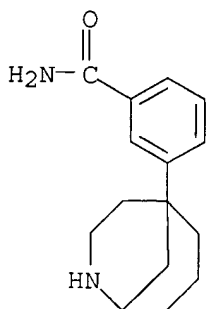
10/762,730



RN 777932-73-7 CAPLUS
CN Methanesulfonamide, N-[3-(2-azabicyclo[3.3.1]non-5-yl)phenyl]- (9CI) (CA INDEX NAME)



RN 777932-74-8 CAPLUS
CN Benzamide, 3-(2-azabicyclo[3.3.1]non-5-yl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

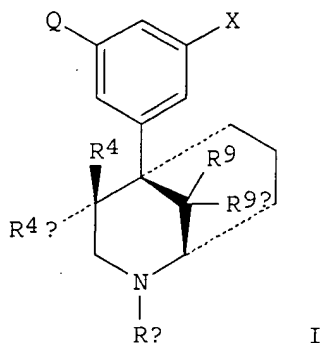
Inventors
L6 ANSWER 2 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:857182 CAPLUS
DOCUMENT NUMBER: 141:350040
TITLE: Preparation of 2-azabicyclo[3.3.1]nonane derivatives as modulators of opioid receptors
INVENTOR(S): Coe, Jotham W.; McHardy, Stanton
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 27 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent

10/762,730

LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004204445	A1	20041014	US 2004-762730	20040122
PRIORITY APPLN. INFO.:			US 2003-462604P	P 20030414
OTHER SOURCE(S):	MARPAT 141:350040			

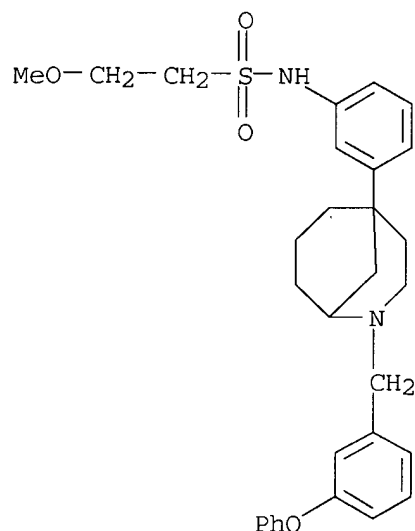
GI



AB The title compds. [I; Ra = H, (CH₂)_nCR₁R₂R₃; X = H, halogen, cyano, -C.tplbond.CR_{3a}, C1-4 alkyl group optionally substituted with from one to three halogen atoms; Q = H, halogen, C1-6 alkyl, cyano, NH₂, NH(C1-4 alkyl), N(C1-4 alkyl)₂, CONH₂, CONH(C1-C4 alkyl), CON(C1-C4 alkyl)₂, -NHCHO, NHCOR₈, NHSO₂R₈; R₁, R₂ = H, , ech (un)substituted C1-6 alkyl, -(CH₂)_j-aryl, -(CH₂)_j-heteroaryl (wherein alkyl, aryl, or heteroaryl is optionally substituted); with the carbon to which R₁ and R₂ are attached, R₁ and R₂ form an (un)substituted C3-7 carbocyclic or 4- to 7-membered heterocyclic group; R₃ is absent or is H, C1-4 alkyl optionally containing one or two unsatd. bonds, OH, C1-4 alkoxy, hydroxy-C1-4 alkyl, (CH₂)_n-NR_{10a}R_{10b}, -(CH₂)_n-NHCO(C1-C4 alkyl), -(CH₂)_n-NO₂, -(CH₂)_n-CN, -(CH₂)_n-CONH₂, (CH₂)_n-CONH(C1-C4 alkyl), -(CH₂)_n-CONR_{10a}R_{10b}; R_{3a} = H, C1-6 alkyl optionally substituted with one or more halogen; R₄, R_{4a}, R₉, R_{9a} = H, C1-4 alkyl, C1-4 alkoxy; R₈ = H, C1-6 alkyl, C3-6 cycloalkyl, aryl, -(C2-C4 alkyl)-O-(C1-4 alkyl), aryl, -(CH₂)_m-NR₁₄R₁₅, 4- to 7-membered heterocyclyl; R_{10a}, R_{10b}, R₁₄, R₁₅ = H, C1-4 alkyl; or R_{10a} and R_{10b} or R₁₄ and R₁₅ connect to form a 4-7 membered heterocyclic ring; R₁₄, R₁₅ = H, C1-C6 alkyl; j, n = independently an integer from 0 to 5] are prepared These compds. bind to and modulate (i.e., inhibit, partially inhibit, activate or partially activate) an opioid receptor or receptors in a mammal, including a human. The subject invention also relates to pharmaceutical compns. comprising such derivs. and methods of using such derivs. to treat disease states, disorders and conditions mediated by opioid receptors, which are selected from the group consisting of irritable bowel syndrome, constipation, nausea, vomiting, pruritic dermatoses, psoriasis, eczema, insect bite, eating disorder, depression, anxiety, schizophrenia, drug addiction, opioid overdose, sexual dysfunction, stroke, head trauma, traumatic brain injury, spinal damage, Parkinson's disease, Alzheimer's disease, age-related cognitive decline and attention deficit, and hyperactivity disorder. In a μ opioid receptor binding assay to rat forebrain tissue, most of the compds. I, e.g. N-[3-(2-cyclopropylmethyl-2-azabicyclo[3.3.1]non-5-yl)phenyl]methanesulfonamide hydrochloride, tested at 100 nM were found to inhibit [3H]-DAMGO binding at the μ opioid receptor in a range of 10-100%.

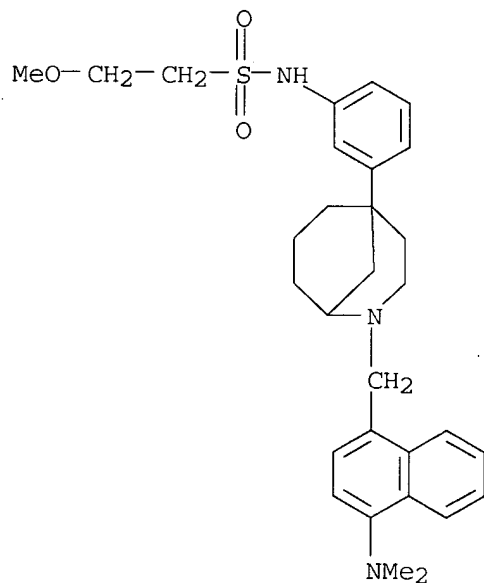
10/762,730

azabicyclo[3.3.1]non-5-yl]phenyl]- (9CI) (CA INDEX NAME)



RN 774241-67-7 CAPLUS

CN Ethanesulfonamide, N-[3-[2-[[4-(dimethylamino)-1-naphthalenyl]methyl]-2-azabicyclo[3.3.1]non-5-yl]phenyl]-2-methoxy- (9CI) (CA INDEX NAME)



L6 ANSWER 3 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:633477 CAPLUS

DOCUMENT NUMBER: 141:150963

TITLE: Sigma-2 receptor agonists and their use in the treatment of immunodeficiency virus infection

INVENTOR(S): Crawford, Keith W.; Bowen, Wayne D.; Hildreth, James E.

PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA

SOURCE: PCT Int. Appl., 73 pp.

CODEN: PIXXD2

10/762,730

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004064775	A2	20040805	WO 2004-US739	20040114
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KR, KR, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI				

PRIORITY APPLN. INFO.: US 2003-440367P P 20030116

AB The invention discloses sigma-2 receptor agonists and their use in the treatment of immunodeficiency virus infections, especially human immunodeficiency virus (HIV) infections. The invention particularly discloses sigma-2 agonists, especially CB-184 and its analogs, that decrease cellular production of sphingomyelin when provided to recipient cells, and inhibit HIV replication.

IT 157752-20-0, CB-64D 165307-47-1, CB-184

165307-47-1D, salts

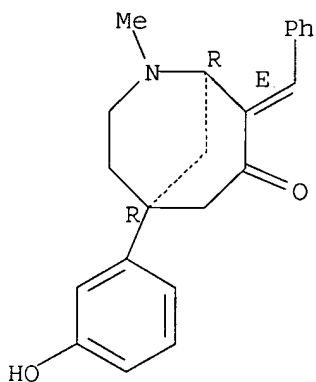
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(sigma-2 receptor agonists for treatment of immunodeficiency virus infection)

RN 157752-20-0 CAPLUS

CN 2-Azabicyclo[3.3.1]nonan-7-one, 5-(3-hydroxyphenyl)-2-methyl-8-(phenylmethylene)-, (1R,5R,8E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

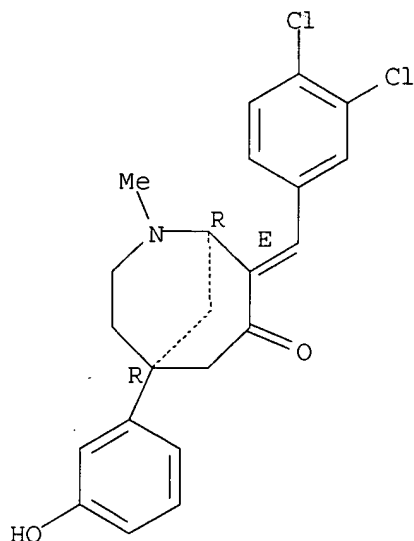


RN 165307-47-1 CAPLUS

CN 2-Azabicyclo[3.3.1]nonan-7-one, 8-[(3,4-dichlorophenyl)methylene]-5-(3-hydroxyphenyl)-2-methyl-, (1R,5R,8E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

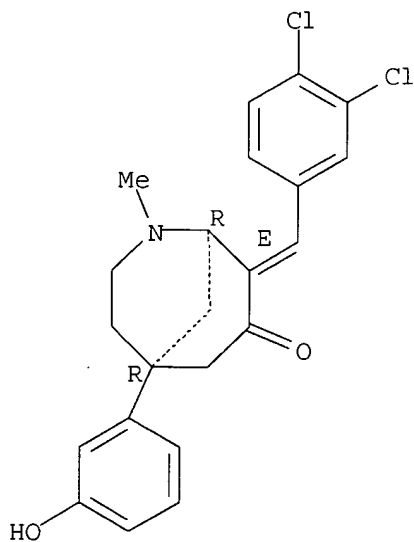
10/762,730



RN 165307-47-1 CAPLUS

CN 2-Azabicyclo[3.3.1]nonan-7-one, 8-[(3,4-dichlorophenyl)methylene]-5-(3-hydroxyphenyl)-2-methyl-, (1R,5R,8E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



L6 ANSWER 4 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:580825 CAPLUS

DOCUMENT NUMBER: 141:199483

TITLE: A critical structural determinant of opioid receptor interaction with phenolic 5-phenylmorphans

AUTHOR(S): Kim, In Jong; Dersch, Christina M.; Rothman, Richard B.; Jacobson, Arthur E.; Rice, Kenner C.

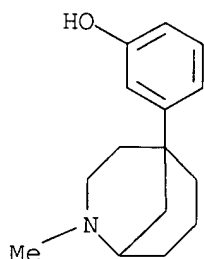
CORPORATE SOURCE: Department of Health and Human Services, Laboratory of Medicinal Chemistry, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, 20892-0815, USA

SOURCE: Bioorganic & Medicinal Chemistry (2004), 12(16), 4543-4550
 CODEN: BMECEP; ISSN: 0968-0896
 PUBLISHER: Elsevier Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English

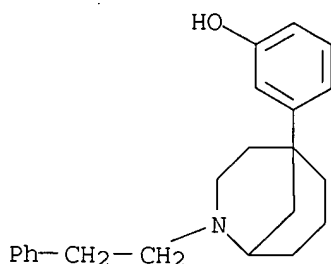
AB The opioid receptor binding affinities of N-methyl- and N-phenethyl-5-phenylmorphans with a meta-hydroxy substituent [3-(2-methyl-2-azabicyclo[3.3.1]non-5-yl)phenol, and 3-(2-phenethyl-2-azabicyclo[3.3.1]non-5-yl)phenol] were compared with the affinities of four new ligands bearing an ortho- or para-hydroxyl substituent [2-(2-methyl-2-azabicyclo[3.3.1]non-5-yl)phenol and 2-(2-phenethyl-2-azabicyclo[3.3.1]non-5-yl)phenol, 4-(2-methyl-2-azabicyclo[3.3.1]non-5-yl)phenol, and 4-(2-phenethyl-2-azabicyclo[3.3.1]non-5-yl)phenol] that were synthesized from 2-bromoanisole or the known 2-methyl-5-phenyl-2-azabicyclo[3.3.1]nonane, resp. The data indicated that either the electronic state of the phenolic ring is critical for the ligand's interaction with an opioid receptor, or that there must be a specific distance and angle for a hydrogen bond between the phenolic moiety and an amino acid in the binding domain that cannot be altered.

IT **27107-68-2 503156-16-9**
 RL: PAC (Pharmacological activity); BIOL (Biological study)
 (critical structural determinant of opioid receptor interaction with phenolic 5-phenylmorphans)

RN 27107-68-2 CAPLUS
 CN Phenol, 3-(2-methyl-2-azabicyclo[3.3.1]non-5-yl)- (9CI) (CA INDEX NAME)

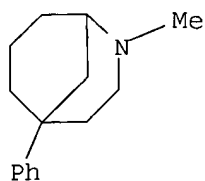


RN 503156-16-9 CAPLUS
 CN Phenol, 3-[2-(2-phenylethyl)-2-azabicyclo[3.3.1]non-5-yl]- (9CI) (CA INDEX NAME)



IT **744220-55-1**
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (critical structural determinant of opioid receptor interaction with phenolic 5-phenylmorphans)

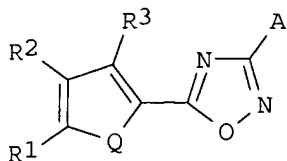
RN 744220-55-1 CAPLUS
 CN 2-Azabicyclo[3.3.1]nonane, 2-methyl-5-phenyl- (9CI) (CA INDEX NAME)



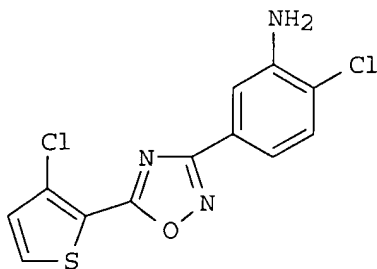
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 2004:565086 CAPLUS
 DOCUMENT NUMBER: 141:123632
 TITLE: Preparation of 3,5-Disubstituted-[1,2,4]-oxadiazoles and analogs as activators of caspases and inducers of apoptosis
 INVENTOR(S): Cai, Sui Xiong; Zhang, Han-zhong; Kuemmerle, Jared D.; Zhang, Hong; Kemnitzer, William E.
 PATENT ASSIGNEE(S): Cytovia, Inc., USA
 SOURCE: PCT Int. Appl., 97 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004058253	A1	20040715	WO 2003-US40308	20031218
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004127521	A1	20040701	US 2003-737865	20031218
PRIORITY APPLN. INFO.:			US 2002-433953P	P 20021218
OTHER SOURCE(S):			MARPAT 141:123632	
GI				



I



II

AB Title compds. I [R1-3 = H, halo, haloalkyl, aryl, etc.; Q = S, O, amino; A = heterocycle, carbocycle] are prepared For instance, 3-amino-4-

10/762,730

chlorobenzamidoxime (preparation given) is reacted with 3-chlorothiophene-2-carbonyl chloride (pyridine, reflux, 50 min) to give II. II and other examples are potent caspase cascade activators and inducers of apoptosis in solid tumor cells, e.g., human breast cancer cell lines T-47D and ZR-75-1.

IT 157752-20-0, CB-64D 165307-47-1, CB-184

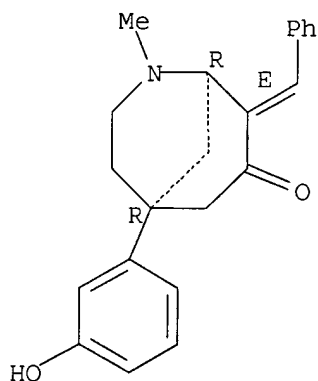
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination pharmaceutical; preparation of 3,5-Disubstituted-[1,2,4]-oxadiazoles and analogs as activators of caspases and inducers of apoptosis)

RN 157752-20-0 CAPLUS

CN 2-Azabicyclo[3.3.1]nonan-7-one, 5-(3-hydroxyphenyl)-2-methyl-8-(phenylmethylene)-, (1R,5R,8E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

Double bond geometry as shown.

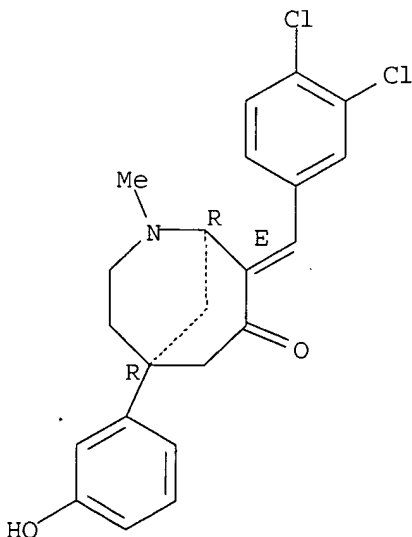


RN 165307-47-1 CAPLUS

CN 2-Azabicyclo[3.3.1]nonan-7-one, 8-[(3,4-dichlorophenyl)methylene]-5-(3-hydroxyphenyl)-2-methyl-, (1R,5R,8E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

Double bond geometry as shown.



10/762,730

ACCESSION NUMBER: 2004:534300 CAPLUS
DOCUMENT NUMBER: 141:65094
TITLE: Substituted 1-benzoyl-3-cyano-pyrrolo[1,2-a]quinolines
and analogs as activators of caspases and inducers of
apoptosis
INVENTOR(S): Cai, Sui Xiong; Drewe, John A.; Jiang, Sungchun;
Kasibhatla, Shailaja; Kuemmerle, Jared Daniel;
Sirisoma, Nilantha Sudath; Zhang, Han-Zhong
PATENT ASSIGNEE(S): Cytovia, Inc., USA
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004055163	A2	20040701	WO 2003-US39550	20031212
WO 2004055163	A3	20040826		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2005014759	A1	20050120	US 2003-733229	20031212
PRIORITY APPLN. INFO.:			US 2002-432608P	P 20021212

OTHER SOURCE(S): MARPAT 141:65094

AB The invention discloses substituted 1-benzoyl-3-cyanopyrrolo[1,2-a]quinolines and analogs thereof. Compds. of the invention are activators of caspases and inducers of apoptosis. Therefore, the compds. of the invention can be used to induce cell death in a variety of clin. conditions in which uncontrolled growth and spread of abnormal cells occurs. Compound prepn is described.

IT 157752-20-0, CB-64D 165307-47-1, CB-184

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(benzoylcyanopyrroloquinolines and analogs as activators of caspases and inducers of apoptosis)

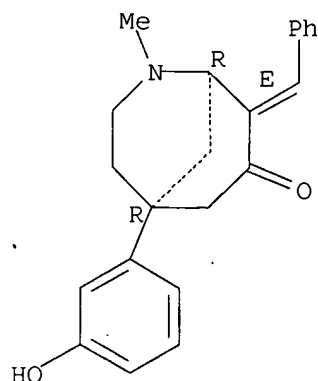
RN 157752-20-0 CAPLUS

CN 2-Azabicyclo[3.3.1]nonan-7-one, 5-(3-hydroxyphenyl)-2-methyl-8-(phenylmethylene)-, (1R,5R,8E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

Double bond geometry as shown.

10/762,730

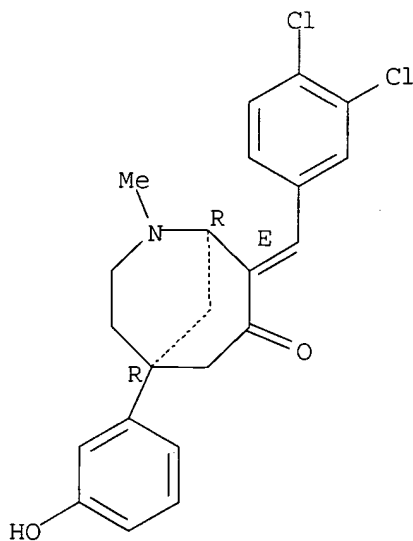


RN 165307-47-1 CAPLUS

CN 2-Azabicyclo[3.3.1]nonan-7-one, 8-[(3,4-dichlorophenyl)methylene]-5-(3-hydroxyphenyl)-2-methyl-, (1R,5R,8E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

Double bond geometry as shown.



L6 ANSWER 7 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:489237 CAPLUS

DOCUMENT NUMBER: 141:100133

TITLE: Sigma-2 receptors are specifically localized to lipid rafts in rat liver membranes

AUTHOR(S): Gebreselassie, Daniel; Bowen, Wayne D.

CORPORATE SOURCE: Unit on Receptor Biochemistry and Pharmacology, Laboratory of Medicinal Chemistry, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, 20892, USA

SOURCE: European Journal of Pharmacology (2004), 493(1-3), 19-28

CODEN: EJPHAZ; ISSN: 0014-2999

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

10/762,730

AB The authors have previously shown that sigma-2 receptors are relatively difficult to solubilize. Rat liver membranes were treated on ice with 1% Triton X-100 or 20 mM 3-[(3-cholamidopropyl)dimethylammonio]-1-propanesulfonate (CHAPS), and the extract subjected to centrifugation on a discontinuous gradient of 5%, 38%, and 40% sucrose. Gradient fractions were analyzed for sigma-1 receptors using [3H](+)-pentazocine and for sigma-2 receptors using [3H]1,3-di-o-tolylguanidine ([3H]DTG), in the presence of dextrallorphan. Flotillin-2 was assessed by immunoblotting as a marker for lipid rafts. Sigma-2 receptors were found to discretely co-localize with flotillin-2 in lipid raft fractions. However, sigma-1 receptors were found throughout the gradient. Rafts prepared in CHAPS had sigma-2 receptors with normal pharmacol. characteristics, whereas those in Triton X-100-prepared rafts had about seven-fold lower affinity for [3H]DTG and other ligands. Thus, sigma-2 receptors are resident in membrane lipid rafts, whereas sigma-1 receptors appear in both raft and non-raft membrane domains. Lipid rafts may play an important role in the mechanism of sigma-2 receptor-induced apoptosis.

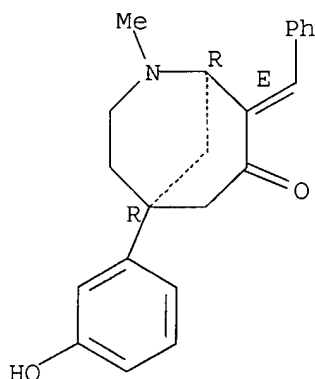
IT 157752-20-0, CB64D

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(sigma-2 receptors are specifically localized to lipid rafts in rat liver membranes)

RN 157752-20-0 CAPLUS

CN 2-Azabicyclo[3.3.1]nonan-7-one, 5-(3-hydroxyphenyl)-2-methyl-8-(phenylmethylene)-, (1R,5R,8E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:20448 CAPLUS

DOCUMENT NUMBER: 140:87676

TITLE: Derivatives of gambogic acid and analogs as activators of caspases and inducers of apoptosis

INVENTOR(S): Tseng, Ben; Sirisoma, Nilantha Sudath; Cai, Sui Xiong; Zhang, Han-Zhong; Kasibhatla, Shailaja; Ollis, Kristin P.; Drewe, John A.

PATENT ASSIGNEE(S): Cytovia, Inc., USA

SOURCE: PCT Int. Appl., 92 pp.

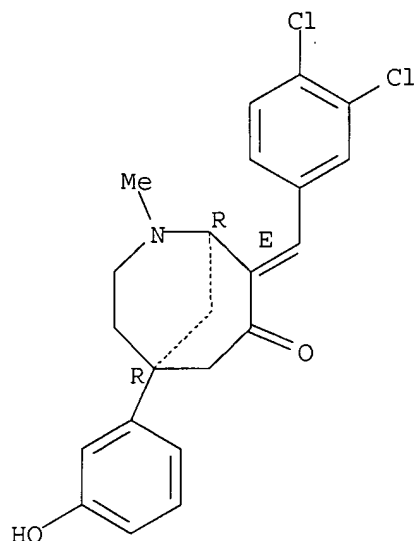
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:



L6 ANSWER 9 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:965570 CAPLUS

DOCUMENT NUMBER: 140:175001

TITLE: Discovery of the First N-Substituted
4 β -Methyl-5-(3-hydroxyphenyl)morphane To Possess
Highly Potent and Selective Opioid δ Receptor
Antagonist Activity

AUTHOR(S): Carroll, F. Ivy; Zhang, Li; Mascarella, S. Wayne;
Navarro, Hernan A.; Rothman, Richard B.; Cantrell,
Buddy E.; Zimmerman, Dennis M.; Thomas, James B.

CORPORATE SOURCE: Chemistry and Life Sciences, Research Triangle
Institute, Research Triangle Park, NC, 27709, USA

SOURCE: Journal of Medicinal Chemistry (2004), 47(2), 281-284
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A structurally novel opioid δ receptor selective antagonist has been identified. This compound, (+)-5-(3-hydroxyphenyl)-4-methyl-2-(3-phenylpropyl)-2-azabicyclo[3.3.1]non-7-yl-(1-phenyl-1-cyclopentane)carboxamide [(+)-KF4], showed a K_e value of 0.15 nM in the [35S]GTP γ S functional assay. (+)-KF4 is also a δ inverse agonist with an IC₅₀ value of 1.8 nM. To the authors knowledge, this is the first potent and selective δ opioid receptor antagonist from the 5-phenylmorphane class of opioids.

IT 658713-91-8P 658713-92-9P 658713-93-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(discovery of first N-substituted methyl(3-hydroxyphenyl)morphane to possess highly potent and selective opioid δ receptor antagonist activity and inverse agonist activity)

RN 658713-91-8 CAPLUS

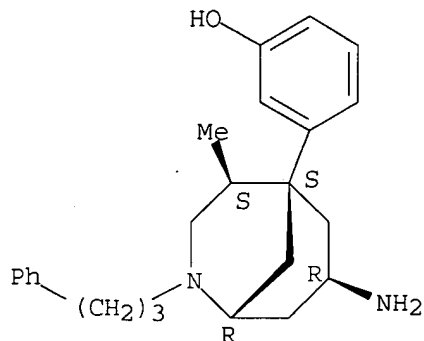
CN Cyclopentanecarboxamide, N-[(1R,4R,5S,6R)-5-(3-hydroxyphenyl)-4-methyl-2-(3-phenylpropyl)-2-azabicyclo[3.3.1]non-6-yl]-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

10/762,730

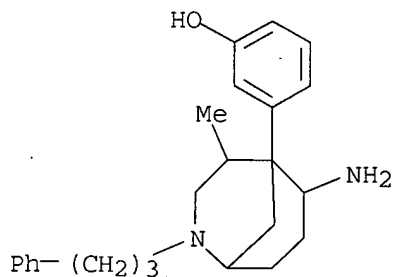
CN Phenol, 3-[(1R,4S,5S,7R)-7-amino-4-methyl-2-(3-phenylpropyl)-2-azabicyclo[3.3.1]non-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 658713-94-1 CAPLUS

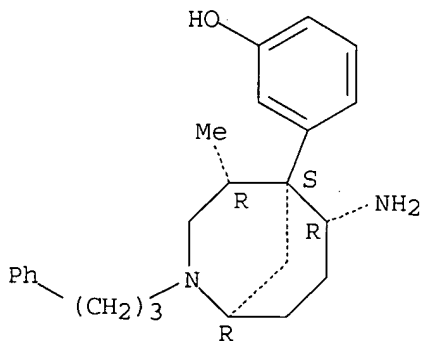
CN Phenol, 3-[6-amino-4-methyl-2-(3-phenylpropyl)-2-azabicyclo[3.3.1]non-5-yl]- (9CI) (CA INDEX NAME)



RN 658713-95-2 CAPLUS

CN Phenol, 3-[(1R,4R,5S,6R)-6-amino-4-methyl-2-(3-phenylpropyl)-2-azabicyclo[3.3.1]non-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT:

33

THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 10 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

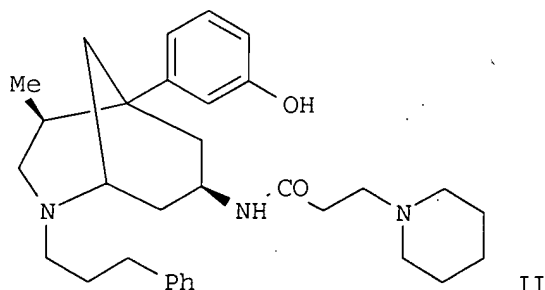
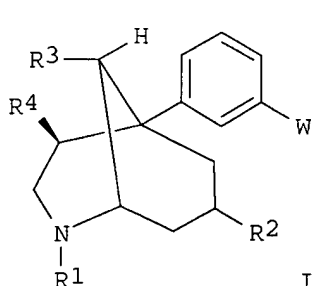
ACCESSION NUMBER: 2003:443323 CAPLUS

DOCUMENT NUMBER: 139:246129

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

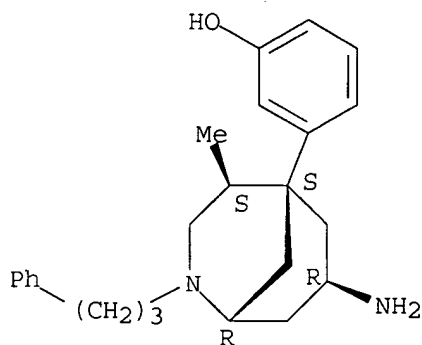
L6 ANSWER 11 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
 L6
 ACCESSION NUMBER: 2002:594678 CAPLUS
 DOCUMENT NUMBER: 137:155089
 TITLE: Preparation of azabicyclononanes for therapeutic use
 as κ opioid receptor ligands for the treatment
 of cocaine or heroin addiction
 INVENTOR(S): Carroll, F. Ivy; Thomas, James B.; Mascarella, S.
 Wayne
 PATENT ASSIGNEE(S): Research Triangle Institute, USA
 SOURCE: PCT Int. Appl., 57 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002060445	A1	20020808	WO 2002-US1231	20020201
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2002143145	A1	20021003	US 2001-774566	20010201
US 6559159	B2	20030506		
CA 2436409	AA	20020808	CA 2002-2436409	20020201
EP 1363629	A1	20031126	EP 2002-704144	20020201
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
JP 2004520383	T2	20040708	JP 2002-560637	20020201
PRIORITY APPLN. INFO.:			US 2001-774566	A 20010201
			WO 2002-US1231	W 20020201
OTHER SOURCE(S):	MARPAT 137:155089			
GI				



AB Structurally novel κ opioid receptor antagonists, such as I [R1 = alkyl, alkenyl, alkynyl, arylalkyl, etc; R2 = acylamino, carbamoyl, carboxyl, aminoalkyl, heterocyclalkyl, etc.; R3 = H, alkyl, alkenyl, alkynyl, arylalkyl, carboxyl; R4 = H, alkyl, alkenyl, alkynyl, arylalkyl;

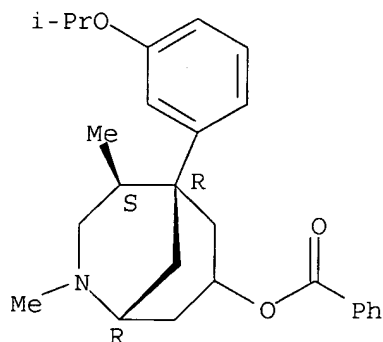
10/762,730



RN 444904-25-0 CAPLUS

CN 2-Azabicyclo[3.3.1]nonan-7-ol, 2,4-dimethyl-5-[3-(1-methylethoxy)phenyl]-, benzoate (ester), (1R,4S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 12 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:583529 CAPLUS

DOCUMENT NUMBER: 138:265113

TITLE: Probes for Narcotic Receptor Mediated Phenomena. Part 28: New Opioid Antagonists from Enantiomeric Analogues of 5-(3-Hydroxyphenyl)-N-phenylethylmorphinan

AUTHOR(S): Hashimoto, Akihiro; Jacobson, Arthur E.; Rothman, Richard B.; Dersch, Christina M.; George, Clifford; Flippen-Anderson, Judith L.; Rice, Kenner C.

CORPORATE SOURCE: National Institute of Diabetes and Digestive and Kidney Diseases, Laboratory of Medicinal Chemistry, National Institutes of Health, Bethesda, MD, 20892-0815, USA

SOURCE: Bioorganic & Medicinal Chemistry (2002), 10(10), 3319-3329

CODEN: BMECEP; ISSN: 0968-0896

PUBLISHER: Elsevier Science Ltd.

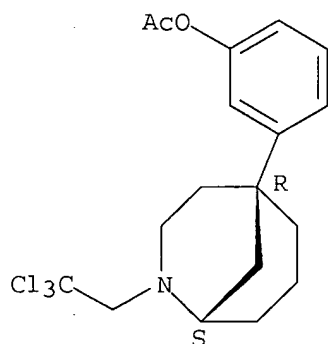
DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 138:265113

AB Enantiomeric analogs of 5-(3-hydroxyphenyl)morphinan ligands were synthesized and evaluated because of our unexpected finding that opioid antagonists can be obtained in the 5-phenylmorphinan series of opioids without sterically hindering the rotation of the phenolic ring. We determined the opioid receptor binding affinity of these new analogs, as well as the

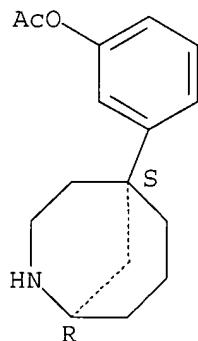
10/762,730



RN 503156-10-3 CAPLUS

CN Phenol, 3-(1R,5S)-2-azabicyclo[3.3.1]non-5-yl-, acetate (ester) (9CI) (CA INDEX NAME)

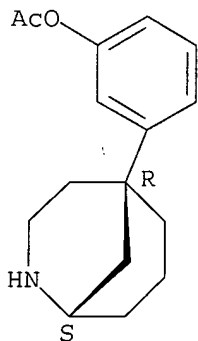
Absolute stereochemistry.



RN 503156-11-4 CAPLUS

CN Phenol, 3-(1S,5R)-2-azabicyclo[3.3.1]non-5-yl-, acetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

21

THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 13 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:509530 CAPLUS

DOCUMENT NUMBER: 137:216844

TITLE: Discovery of an Opioid κ Receptor Selective Pure

10/762,730

Antagonist from a Library of N-Substituted
4 β -Methyl-5-(3-hydroxyphenyl)morphans

AUTHOR(S): Thomas, James B.; Atkinson, Robert N.; Namdev,
Nivedita; Rothman, Richard B.; Gigstad, Kenneth M.;
Fix, Scott E.; Mascarella, S. Wayne; Burgess, Jason
P.; Vinson, N. Ariane; Xu, Heng; Dersch, Christina M.;
Cantrell, Buddy E.; Zimmerman, Dennis M.; Carroll, F.
Ivy

CORPORATE SOURCE: Chemistry and Life Sciences, Research Triangle
Institute, Research Triangle Park, NC, 27709, USA

SOURCE: Journal of Medicinal Chemistry (2002), 45(16),
3524-3530
CODEN: JMCMAR; ISSN: 0022-2623

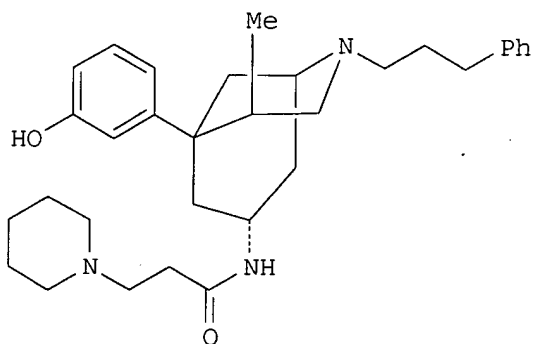
PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 137:216844

GI



AB A library of compds. biased toward opioid receptor antagonist activity was prepared by incorporating N-phenylpropyl-4 β -methyl-5-(3-hydroxyphenyl)morphans as the core scaffold using simultaneous solution phase synthetic methodol. From this library, N-phenylpropyl-4 β -methyl-5-(3-hydroxyphenyl)-7 α -[3-(1-piperidinyl)propanamido]morphane (I) was identified as the first potent and selective κ opioid receptor antagonist from the 5-phenylmorphane class of opioids.

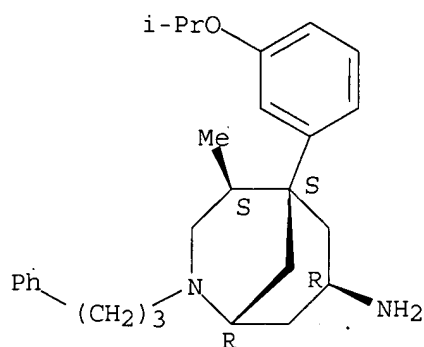
IT **455311-44-1P 455311-45-2P 455311-46-3P**
RL: PAC (Pharmacological activity); PNU (Preparation, unclassified); BIOL (Biological study); PREP (Preparation)
(discovery of an opioid κ receptor selective pure antagonist from a library of N-substituted 4 β -methyl-5-(3-hydroxyphenyl)morphans)

RN 455311-44-1 CAPLUS

CN Butanamide, 4-(dimethylamino)-N-[(1S,4R,5R,7S)-5-(3-hydroxyphenyl)-4-methyl-2-(3-phenylpropyl)-2-azabicyclo[3.3.1]non-7-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

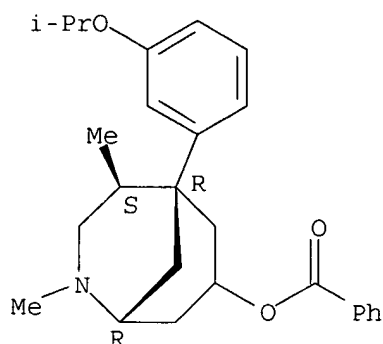
10/762,730



RN 444904-25-0 CAPLUS

CN 2-Azabicyclo[3.3.1]nonan-7-ol, 2,4-dimethyl-5-[3-(1-methylethoxy)phenyl]-, benzoate (ester), (1R,4S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 14 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:70938 CAPLUS

DOCUMENT NUMBER: 136:363394

TITLE: Sigma-2 receptor agonists activate a novel apoptotic pathway and potentiate antineoplastic drugs in breast tumor cell lines

AUTHOR(S): Crawford, Keith W.; Bowen, Wayne D.

CORPORATE SOURCE: Department of Pharmacology, Howard University College of Medicine, Washington, DC, 20059, USA

SOURCE: Cancer Research (2002), 62(1), 313-322

CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We have reported previously that sigma-2 receptors are expressed in high densities in a variety of tumor cell types and that various sigma ligands have cytotoxic effects. Other investigators have demonstrated increased expression of sigma-2 receptors in rapidly proliferating tumors and the ability of some sigma ligands to inhibit proliferation. We demonstrate here the ability of sigma-2 receptor agonists to induce cell death by a mechanism consistent with apoptosis. In breast tumor cell lines that are sensitive (MCF-7) and resistant (MCF-7/Adr-, T47D, and SKBr3) to antineoplastic agents, incubation with the sigma-2 subtype-selective agonists CB-64D and CB-184 produced dose-dependent cytotoxicity (measured by lactate dehydrogenase release into medium). The EC50 for this response

L6 ANSWER 15 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:833074 CAPLUS
DOCUMENT NUMBER: 135:366722
TITLE: Potentiation of antineoplastic agents using sigma-2
ligands
INVENTOR(S): Crawford, Keith W.; Bowen, Wayne D.
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

OTHER SOURCE(S): MARPAT 135:366722

AB The invention discloses the use of sigma-2 agonists to potentiate the activity of antineoplastic agents. These substances are useful for treating cancerous tumors and, in particular, drug-resistant tumors in humans. Methods for sensitizing multidrug resistant cells to antitumor agents comprising contacting the cells with a sigma-2 agonist are also

10/762,730

described.

IT 157752-20-0, CB 64D 165307-47-1, CB 184

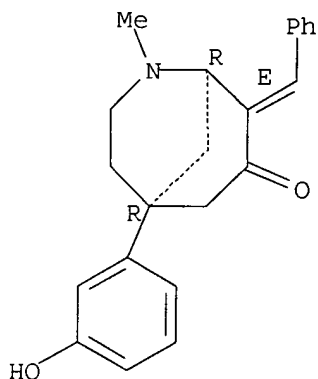
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(sigma-2 agonist for antineoplastic agent potentiation)

RN 157752-20-0 CAPLUS

CN 2-Azabicyclo[3.3.1]nonan-7-one, 5-(3-hydroxyphenyl)-2-methyl-8-(phenylmethylene)-, (1R,5R,8E)- (9CI) (CA INDEX NAME)

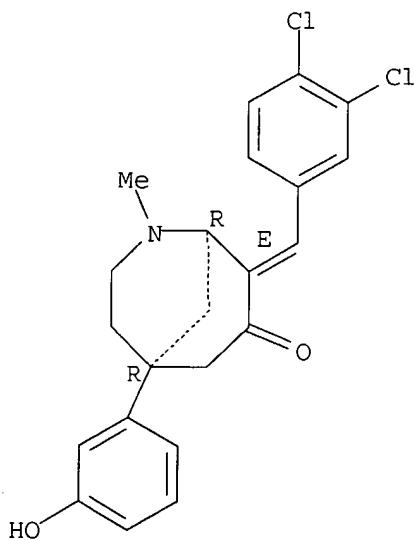
Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



RN 165307-47-1 CAPLUS

CN 2-Azabicyclo[3.3.1]nonan-7-one, 8-[(3,4-dichlorophenyl)methylene]-5-(3-hydroxyphenyl)-2-methyl-, (1R,5R,8E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



L6 ANSWER 16 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:892230 CAPLUS

DOCUMENT NUMBER: 134:231497

TITLE: Opioid peptide receptor studies. 14. Stereochemistry determines agonist efficacy and intrinsic efficacy in

the [35S]GTP- γ -S functional binding assay

AUTHOR(S): Xu, Heng; Hashimoto, Akihiro; Rice, Kenner C.; Jacobson, Arthur E.; Thomas, James B.; Carroll, F. Ivy; Lai, Josephine; Rothman, Richard B.

CORPORATE SOURCE: CPS, DIR, NIDA, Baltimore, MD, 21224, USA

SOURCE: Synapse (New York) (2001), 39(1), 64-69
CODEN: SYNAET; ISSN: 0887-4476

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

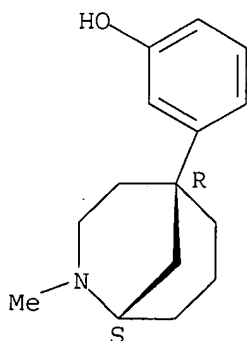
AB Previous data obtained with the cloned rat μ opioid receptor demonstrated that stereochem. affects the four parameters of the ligand-receptor interaction: potency (ED50), efficacy (maximal stimulation), intrinsic efficacy (effect as a function of receptor occupation), and binding affinity. This study evaluated the activities of structurally diverse opioid receptor ligands in the [35S]GTP- γ -S binding assay, comparing the relationship between receptor binding, activation, efficacy, and intrinsic efficacy. The data, obtained with cloned rat μ receptors, demonstrated that an analgetic, (-)-5-m-hydroxyphenyl-2-methylmorphinan (NIH8508), and its (+)-isomer (NIH8509), behave as partial agonists, but had different intrinsic efficacy in the [35S]GTP- γ -S binding assay. Replacement of the Me group with the phenethyl group on the piperidine nitrogen of NIH8508 and NIH8509 [(1R,5S)-AH019 and (1S,5R)-AH019] increased affinity for the μ receptor and eliminated any agonist effect, supporting the hypothesis that certain structural features make these compds. antagonists. These study also show that all of the fully efficacious μ agonists studied here had high levels of intrinsic efficacy, producing a 50% response at about 10% receptor occupancy. Comparison of the binding K_i in competitively inhibiting [¹²⁵I]OXY binding to the functional K_i for opioid antagonists [K_i (IOXY)/ K_i (GTP- γ -S)] provides more detailed evidence that the [35S]GTP- γ -S binding assay can be used to reliably determine apparent functional antagonist K_i values in addition to agonist ED50, efficacy and intrinsic efficacy.

IT 28623-81-6, NIH 8509 28623-84-9, NIH 8508
330625-46-2, (1R,5S)-AH 019 330625-47-3, (1S,5R)-AH 019
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(opioid peptide receptor studies. 14. stereochem. dets. agonist efficacy and intrinsic efficacy in the [35S]GTP- γ -S functional binding assay)

RN 28623-81-6 CAPLUS

CN Phenol, 3-[(1S,5R)-2-methyl-2-azabicyclo[3.3.1]non-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 28623-84-9 CAPLUS

L6 ANSWER 17 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:171768 CAPLUS

DOCUMENT NUMBER: 132:318283

TITLE: Modulation of cellular calcium by sigma-2 receptors: release from intracellular stores in human SK-N-SH neuroblastoma cells

AUTHOR(S): Vilner, Bertold J.; Bowen, Wayne D.

CORPORATE SOURCE: Unit on Receptor Biochemistry and Pharmacology, Laboratory of Medicinal Chemistry, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, USA

SOURCE: Journal of Pharmacology and Experimental Therapeutics (2000), 292(3), 900-911

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Human SK-N-SH neuroblastoma cells expressed sigma-1 and sigma-2 receptors with similar pharmacol. profiles to those of rodent-derived tissues, although sigma-2 receptors exhibited some affinity differences that might suggest heterogeneity or species differences. Structurally diverse sigma ligands produced two types of increases in intracellular (cytosolic) Ca²⁺ concentration ([Ca²⁺]_i) in these cells. CB-64D, CB-64L, JL-II-147, BD737, LR172,

BD1008, haloperidol, reduced haloperidol, and ibogaine all produced an immediate, dose-dependent, and transient rise in [Ca²⁺]_i. Sigma-inactive compds. structurally similar to the most active sigma ligands and ligands for several neurotransmitter receptors produced little or no effect. The high activity of CB-64D and ibogaine (sigma-2-selective ligands) compared with the low activity of (+)-pentazocine and other (+)-benzomorphans (sigma-1-selective ligands), in addition to enantioselectivity for CB-64D over CB-64L, strongly indicated mediation by sigma-2 receptors. The effect of CB-64D and BD737 was blocked by the sigma antagonists BD1047 and BD1063, further confirming specificity as a receptor-mediated event. The transient rise in [Ca²⁺]_i occurred in the absence of extracellular Ca²⁺ and was completely eliminated by pretreatment of cells with thapsigargin. Thus, sigma-2 receptors stimulate a transient release of Ca²⁺ from the endoplasmic reticulum. Prolonged exposure of cells to sigma-receptor ligands resulted in a latent and sustained rise in [Ca²⁺]_i, with a pharmacol. profile identical to that of the transient rise. This sustained rise in [Ca²⁺]_i was affected by neither the removal of extracellular Ca²⁺ nor thapsigargin pretreatment, suggesting latent sigma-2 receptor-induced release from thapsigargin-insensitive intracellular Ca²⁺ stores. Sigma-2 receptors may use Ca²⁺ signals in producing cellular effects.

IT 157752-18-6, CB 64L 266691-71-8, CB 53D

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(modulation of cellular calcium by σ -2 receptors: release from intracellular stores in human SK-N-SH neuroblastoma cells)

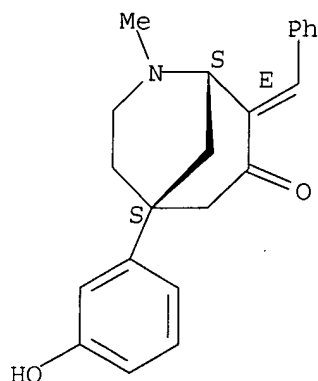
RN 157752-18-6 CAPLUS

CN 2-Azabicyclo[3.3.1]nonan-7-one, 5-(3-hydroxyphenyl)-2-methyl-8-(phenylmethylene)-, (1S,5S,8E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

Double bond geometry as shown.

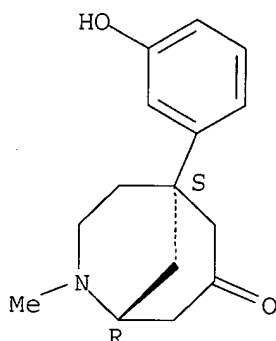
10/762,730



RN 266691-71-8 CAPLUS

CN 2-Azabicyclo[3.3.1]nonan-7-one, 5-(3-hydroxyphenyl)-2-methyl-, (1R,5S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L6 ANSWER 18 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:594935 CAPLUS

DOCUMENT NUMBER: 131:228652

TITLE: Preparation of substituted piperidines for
pharmaceutical use as opioid antagonists

INVENTOR(S): Carroll, Frank Ivy

PATENT ASSIGNEE(S): USA

SOURCE: PCT Int. Appl., 171 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9945925	A1	19990916	WO 1999-US5131	19990309
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,			

CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2324418	AA	19990916	CA 1999-2324418	19990309
AU 9930738	A1	19990927	AU 1999-30738	19990309
AU 756983	B2	20030130		
EP 1061919	A1	20001227	EP 1999-912345	19990309
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002506032	T2	20020226	JP 2000-535340	19990309
US 2002165396	A1	20021107	US 2002-100097	20020319
US 6552032	B2	20030422		
US 2002169324	A1	20021114	US 2002-100096	20020319
US 6593348	B2	20030715		
US 2002193602	A1	20021219	US 2002-99948	20020319
US 6531481	B2	20030311		
US 2003158415	A1	20030821	US 2002-266774	20021009
US 2004146518	A1	20040729	US 2003-742782	20031223
PRIORITY APPLN. INFO.:			US 1998-77402P	P 19980310
			US 1998-107902P	P 19981110
			WO 1999-US5131	W 19990309
			US 2000-623872	A3 20001127
			US 2002-99948	A1 20020319
OTHER SOURCE(S):	MARPAT 131:228652			
GI				

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

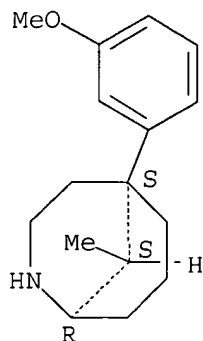
AB Piperidine containing heterocyclic compds. I [R1, R2 = H, alkyl, aryl, arylalkyl; R3 = alkyl, cycloalkyl, aryl, arylalkyl, etc.], II [R1 = alkyl, arylalkyl; R3, R4, R5, R6 = H, OH, NH2, CN, CF3, CN, NO2, alkyl, alkyloxy, halogen, amino, etc.; R7 = H, alkyl], and III [R1 = alkyl, arylalkyl; R2 = H, NH2, :O, alkyl, arylalkyl, amino, etc.] were prepared for use as opioid antagonists to treat a variety of disease states which involve the opioid receptors. Thus, the hydrochloride salt of piperidine IV [R3 = (CH2)2C6H4-4-OH], i.e. RTI 5989-29, was prepared starting from (+)-(3R,4R)-dimethyl-4-(3-hydroxyphenyl)piperidine, N-(tert-butoxycarbonyl)-L-valine, and 3-(4-hydroxyphenyl)propanoic acid. The prepared heterocyclic compds. containing a piperidine subunit were tested for κ -, μ -, and δ -opioid receptor binding activity.

IT **244048-54-2P**
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
 (preparation of heterocyclic compds. containing a piperidine subunit for pharmaceutical use as opioid antagonists)

RN 244048-54-2 CAPLUS

CN Phenol, 3-[(1R,5S,9S)-2,9-dimethyl-2-azabicyclo[3.3.1]non-5-yl]-, rel-(9CI) (CA INDEX NAME)

Relative stereochemistry.

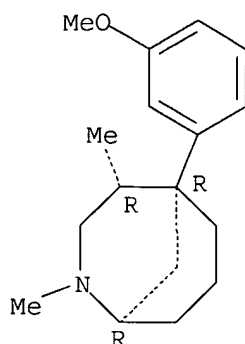


REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 19 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
 J
 ACCESSION NUMBER: 1999:98322 CAPLUS
 DOCUMENT NUMBER: 130:182632
 TITLE: A stereoselective synthetic approach to N-alkyl-4 β -methyl-5-phenylmorphans
 AUTHOR(S): Thomas, James B.; Gigstad, Kenneth M.; Fix, Scott E.; Burgess, Jason P.; Cooper, Julie B.; Mascarella, S. Wayne; Cantrell, Buddy E.; Zimmerman, Dennis M.; Carroll, F. Ivy
 CORPORATE SOURCE: Chemistry and Life Sciences, Research Triangle Institute, Research Triangle Park, NC, 27709, USA
 SOURCE: Tetrahedron Letters (1999), 40(3), 403-406
 CODEN: TELEAY; ISSN: 0040-4039
 PUBLISHER: Elsevier Science Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 130:182632
 AB A convergent, highly stereoselective synthetic approach to N-alkyl-4 β -methyl-5-phenylmorphans has been developed utilizing alkylation of the metalloenamine of N-alkyl-1,2,3,6-tetrahydro-4-phenylpyridines with 2-(chloromethyl)-3,5-dioxahex-1-ene (Okahara's reagent) followed by Clemmensen reduction
 IT **220503-24-2P**
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (a stereoselective synthetic approach to N-alkyl-4 β -methyl-5-phenylmorphans)
 RN 220503-24-2 CAPLUS
 CN 2-Azabicyclo[3.3.1]nonane, 5-(3-methoxyphenyl)-2,4-dimethyl-, (1R,4R,5R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

10/762,730



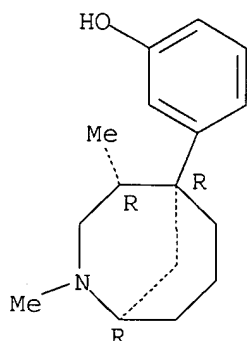
IT 220503-21-9P

RL: SPN (Synthetic preparation); PREP (Preparation)
(a stereoselective synthetic approach to N-alkyl-4 β -methyl-5-phenylmorphans)

RN 220503-21-9 CAPLUS

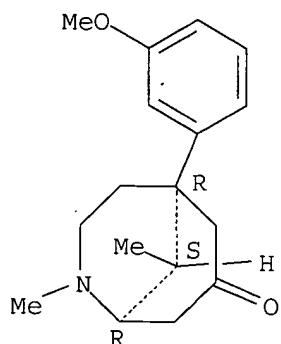
CN Phenol, 3-[(1R,4R,5R)-2,4-dimethyl-2-azabicyclo[3.3.1]non-5-yl]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 20 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:603858 CAPLUS
DOCUMENT NUMBER: 129:316409
TITLE: Synthesis of 9 β -methyl-2-alkyl-7-oxo-5-arylmorphans
AUTHOR(S): Thomas, James B.; Zheng, Xiaoling; Brieady, Lawrence E.; Burgess, Jason P.; Mascarella, S. Wayne; Fix, Scott E.; Cantrell, Buddy E.; Zimmerman, Dennis M.; Carroll, F. Ivy
CORPORATE SOURCE: Chem. Life Sci., Res. Triangle Inst., Research Triangle Park, NC, 27709, USA
SOURCE: Tetrahedron Letters (1998), 39(39), 7001-7004
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 129:316409
AB A convergent synthetic approach to 9 β -methyl-2-alkyl-7-oxo-5-arylmorphans has been developed utilizing alkylation of the metalloenamine of 1,2,3,6-tetrahydro-4-aryl-1-alkylpyridines with 2-(chloromethyl)-3,5-



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 21 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 1998:600696 CAPLUS
 DOCUMENT NUMBER: 129:325731
 TITLE: N-Substituted 9 β -Methyl-5-(3-hydroxyphenyl)morphans Are Opioid Receptor Pure Antagonists
 AUTHOR(S): Thomas, James B.; Zheng, Xiaoling; Mascarella, S. Wayne; Rothman, Richard B.; Dersch, Christina M.; Partilla, John S.; Flippen-Anderson, Judith L.; George, Clifford F.; Cantrell, Buddy E.; Zimmerman, Dennis M.; Carroll, F. Ivy
 CORPORATE SOURCE: Chemistry and Life Sciences, Research Triangle Institute, Research Triangle Park, NC, 27709, USA
 SOURCE: Journal of Medicinal Chemistry (1998), 41(21), 4143-4149
 CODEN: JMCMAR; ISSN: 0022-2623
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB The inhibition of radioligand binding and [35S]GTP γ S functional assay data for N-methyl- and N-phenethyl-9 β -methyl-5-(3-hydroxyphenyl)morphans (I and II) show that these compds. are pure antagonists at the μ , δ , and κ opioid receptors. Since I and II have the 5-(3-hydroxyphenyl) group locked in a conformation comparable to an equatorial group of a piperidine chair conformation, this information provides very strong evidence that opioid antagonists can interact with opioid receptors in this conformation. In addition, it suggests that the trans-3,4-dimethyl-4-(3-hydroxyphenyl)piperidine class of antagonist operates via a Ph equatorial piperidine chair conformation. Importantly, the close relationship between the 4-(3-hydroxyphenyl)piperidines and 5-(3-hydroxyphenyl)morphan antagonists shows that the latter class of compound provides a rigid platform on which to build a novel series of opioid antagonists.

IT 215124-71-3P 215124-72-4P

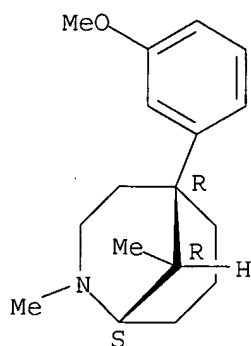
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation and opioid receptor antagonist activity of N-substituted 9 β -methyl-5-(3-hydroxyphenyl)morphans)

RN 215124-71-3 CAPLUS

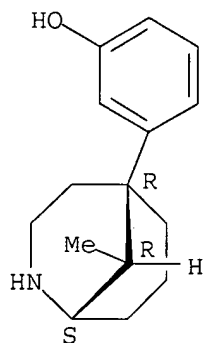
CN Phenol, 3-[(1R,5S,9S)-2,9-dimethyl-2-azabicyclo[3.3.1]non-5-yl]-, hydrochloride, rel- (9CI) (CA INDEX NAME)

10/762,730



RN 215124-76-8 CAPLUS
CN Phenol, 3-[(1R,5S,9S)-9-methyl-2-azabicyclo[3.3.1]non-5-yl]-, rel- (9CI)
(CA INDEX NAME)

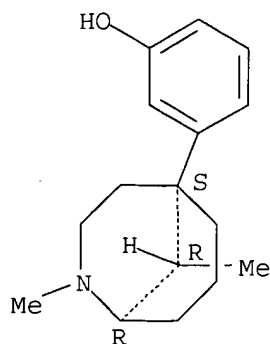
Relative stereochemistry.



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

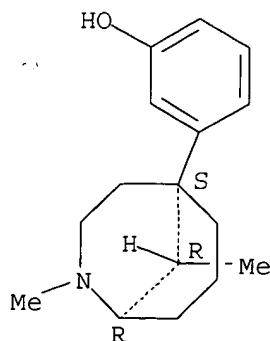
f L6 ANSWER 22 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:482972 CAPLUS
DOCUMENT NUMBER: 125:185593
TITLE: Dependence studies of new compounds in the rhesus monkey, rat and mouse (1995)
AUTHOR(S): Aceto, M. D.; Bowman, E. R.; Harris, L. S.; May, E. L.
CORPORATE SOURCE: Medical College Virginia, Virginia Commonwealth University, Richmond, VA, USA
SOURCE: NIDA Research Monograph (1996), 162(Problems of Drug Dependence, 1995), 408-451
CODEN: MIDAD4; ISSN: 0361-8595
PUBLISHER: National Institute on Drug Abuse
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The ability of a series of drugs to produce dependence was studied in rhesus monkeys, rats, and mice.
IT 88550-29-2
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (dependence studies of new compds. in rhesus monkey and rat and mouse)
RN 88550-29-2 CAPLUS
CN Phenol, 3-(2,9-dimethyl-2-azabicyclo[3.3.1]non-5-yl)-, anti- (9CI) (CA INDEX NAME)

Relative stereochemistry.



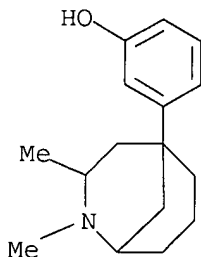
L6 ANSWER 23 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 1996:482970 CAPLUS
 DOCUMENT NUMBER: 125:185591
 TITLE: Biological evaluation of compounds for their physical dependence potential and abuse liability. XIX. Drug evaluation committee of the College on Problems of Drug Dependence, Inc. (1995)
 AUTHOR(S): Jacobson, A. E.
 CORPORATE SOURCE: Laboratory Medicinal Chemistry, National Institute Diabetes Digestive Kidney Diseases, Bethesda, MD, USA
 SOURCE: NIDA Research Monograph (1996), 162 (Problems of Drug Dependence, 1995), 363-376
 CODEN: MIDAD4; ISSN: 0361-8595
 PUBLISHER: National Institute on Drug Abuse
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The phys. dependence potential and abuse liability of various analgesics and stimulants and depressants is described and related to their biol. activities.
 IT **88550-29-2**
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (biol. evaluation of compds. for phys. dependence potential and abuse liability of analgesics and stimulants and depressants)
 RN 88550-29-2 CAPLUS
 CN Phenol, 3-(2,9-dimethyl-2-azabicyclo[3.3.1]non-5-yl)-, anti- (9CI) (CA INDEX NAME)

Relative stereochemistry.



10/762,730

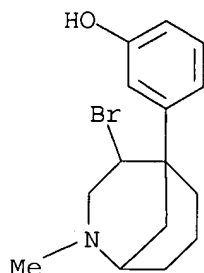
L6 ANSWER 24 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:350730 CAPLUS
DOCUMENT NUMBER: 125:132417
TITLE: Biological evaluation of compounds for their physical
dependence potential and abuse liability. XVII. Drug
Evaluation Committee of the College on Problems of
Drug Dependence, Inc. (1993)
AUTHOR(S): Jacobson, A. E.
CORPORATE SOURCE: USA
SOURCE: NIDA Research Monograph (1994), 140(Problems of Drug
Dependence 1993, Vol. 1), 179-195
CODEN: MIDAD4; ISSN: 0361-8595
PUBLISHER: National Institute on Drug Abuse
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The Drug Evaluation Committee (DEC) of the CPDD (Dr. T. Cicero, Chairman)
is charged with the responsibility of determining the phys. dependence
potential
and abuse liability of potential analgesics, stimulants, and depressants,
and with associated methodol. research. The drugs are obtained from
investigators in universities, industrial groups, and the public sector.
The testing function is carried out under the auspices of the CPDD as a
public service and has provided information to pharmaceutical industry and
governmental agencies for the appropriate scheduling of a drug with the
potential for abuse. The information which DEC provides to university
researchers, who frequently work under a NIDA grant, is useful for determining
the desirability of structural modification of a drug and the DEC biol.
data are often needed for publication of their work in medicinal chemical
journals. Data are reported for 61 compds.
IT 178896-97-4, NIH 10779 178935-97-2, NIH 10778
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or
effector, except adverse); BSU (Biological study, unclassified); BIOL
(Biological study)
(biol. evaluation of drugs for their phys. dependence potential and
abuse liability)
RN 178896-97-4 CAPLUS
CN Phenol, 3-(2,3-dimethyl-2-azabicyclo[3.3.1]non-5-yl)-, hydrochloride (9CI)
(CA INDEX NAME)



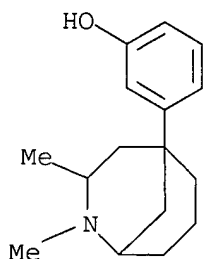
● HCl

RN 178935-97-2 CAPLUS
CN Phenol, 3-(4-bromo-2-methyl-2-azabicyclo[3.3.1]non-5-yl)- (9CI) (CA INDEX
NAME)

10/762,730



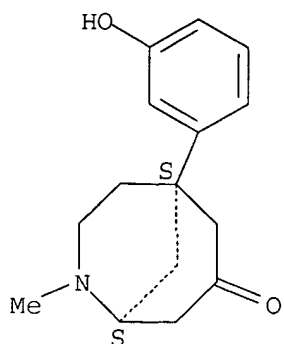
L6 ANSWER 25 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:343479 CAPLUS
DOCUMENT NUMBER: 125:104826
TITLE: Dependence studies of new compounds in the rhesus monkey, rat and mouse (1994)
AUTHOR(S): Aceto, M.D.; Bowman, E.R.; Harris, L.S.; May, E.L.
CORPORATE SOURCE: USA
SOURCE: NIDA Research Monograph (1995), 152(Problems of Drug Dependence 1994, Vol. 1), 162-212
CODEN: MIDAD4; ISSN: 0361-8595
PUBLISHER: National Institute on Drug Abuse
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Twenty-eight compds. were examined in rhesus monkey, rat, and mouse for antinociceptive activity, ability to substitute for morphine, and development of phys. dependence. The data acquired were compared with several standard drugs.
IT 178896-97-4, NIH 10779
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(dependence studies of new compds. in the rhesus monkey, rat and mouse)
RN 178896-97-4 CAPLUS
CN Phenol, 3-(2,3-dimethyl-2-azabicyclo[3.3.1]non-5-yl)-, hydrochloride (9CI)
(CA INDEX NAME)



● HCl

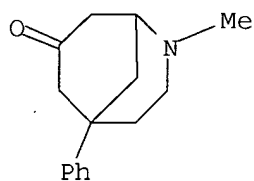
L6 ANSWER 26 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:241972 CAPLUS
DOCUMENT NUMBER: 124:343158
TITLE: Probes for Narcotic Receptor-Mediated Phenomena. 21.
Novel Derivatives of 3-(1,2,3,4,5,11-Hexahydro-3-

10/762,730



RN 176699-46-0 CAPLUS

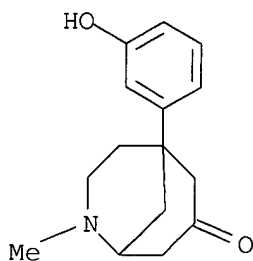
CN 2-Azabicyclo[3.3.1]nonan-7-one, 2-methyl-5-phenyl-, hydrobromide (9CI)
(CA INDEX NAME)



● HBr

RN 176699-47-1 CAPLUS

CN 2-Azabicyclo[3.3.1]nonan-7-one, 5-(3-hydroxyphenyl)-2-methyl-,
hydrobromide (9CI) (CA INDEX NAME)



● HBr

L6 ANSWER 27 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1995:905946 CAPLUS

DOCUMENT NUMBER: 123:305990

TITLE: (E)-8-Benzylidene Derivatives of 2-Methyl-5-(3-hydroxyphenyl)morphans: Highly Selective Ligands for the σ_2 Receptor Subtype

AUTHOR(S): Bertha, Craig M.; Vilner, Bertold J.; Mattson, Mariena V.; Bowen, Wayne D.; Becketts, Karen; Xu, Heng; Rothman, Richard B.; Flippen-Anderson, Judith L.;

CORPORATE SOURCE: Rice, Kenner C.
 Laboratory of Medicinal Chemistry, National Institute
 of Diabetes and Digestive and Kidney Diseases,
 Bethesda, MD, 20892, USA

SOURCE: Journal of Medicinal Chemistry (1995), 38(24), 4776-85
 CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The determination of the structure and function of the σ receptor subtypes and their physiol. role(s) has been impeded by the unavailability of selective ligands. We have developed a new class of σ subtype selective receptor ligands that are (E)-8-benzylidene derivs. of the synthetic opioid (\pm)-, (+)-, and (-)-2-methyl-5-(3-hydroxyphenyl)morphans (1). The derivs. can be prepared by reaction of 1, (+)-1, and (-)-1 with the appropriate benzaldehyde under Claisen-Schmidt conditions. Incorporation of substituted (E)-8-benzylidene moieties onto the 7-keto precursor of (+)-2-methyl-5-(3-hydroxyphenyl)morphane, (+)-1, produces compds. which have between a 25- and 131-fold increase in affinity for the σ_1 receptor subtype relative to the keto precursor (+)-1 (K_i = 762 nM, σ_1). Substitution of an (E)-8-benzylidene moiety onto the 7-keto precursor of (-)-2-methyl-5-(3-hydroxyphenyl)morphane, (-)-1, produces compds. which have at least a 475-3906-fold increase in affinity for the σ_2 receptor subtype relative to the keto precursor (-)-1 (K_i = 25 + 103 nM). This enhancement of σ_2 receptor affinity is accompanied by substantial selectivity of all of these dextrorotatory products for the σ_2 relative to the σ_1 subtype (32-238-fold), and thus, they are among the most σ_2 subtype selective compds. currently known. Furthermore, the σ_1 subtype is highly enantioselective for the levorotatory isomers (41-1034-fold), whereas the σ_2 subtype is only somewhat enantioselective for the dextrorotatory isomers (2.6-9.3-fold). All of these derivs. retain substantial affinity for the μ opioid receptor. Despite the high affinity of the dextrorotatory derivs. for the μ opioid receptor, the high affinity and selectivity for σ_2 over σ_1 sites will surely prove beneficial as tools for the delineation of the function and physiol. role of σ_2 receptors.

IT 157752-16-4 157752-17-5 162060-90-4

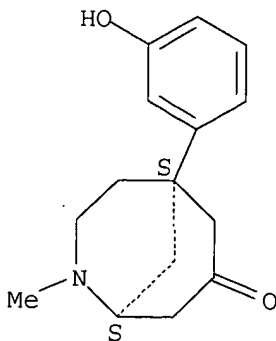
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)

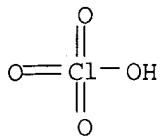
(preparation of (E)-8-benzylidene derivs. of 2-methyl-5-(3-hydroxyphenyl)morphans as selective ligands for σ_2 receptor)

RN 157752-16-4 CAPLUS

CN 2-Azabicyclo[3.3.1]nonan-7-one, 5-(3-hydroxyphenyl)-2-methyl-, (1S)- (9CI)
 (CA INDEX NAME)

Absolute stereochemistry.





L6 ANSWER 28 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1995:792484 CAPLUS

DOCUMENT NUMBER: 123:218718

TITLE: Ligand selectivity of cloned human and rat opioid Mu receptors

AUTHOR(S): Brothman, Richard B.; Xu, Heng; Wang, Jia Bei; Partilla, John S.; Kayakiri, Hiroshi; Rice, Kenner C.; Uhl, George R.

CORPORATE SOURCE: Clinical Psychopharmacology Section, Laboratory of Medicinal Chemistry, Baltimore, MD, 21224, USA

SOURCE: Synapse (New York) (1995), 21(1), 60-4

CODEN: SYNAET; ISSN: 0887-4476

PUBLISHER: Wiley-Liss

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Opiate receptors play major roles in analgesic and euphoric effects of opiate drugs. Recent cloning of cDNAs encoding the rodent and human μ receptor revealed high homol. between the predicted receptors but also some sequence differences. To determine if these sequence differences produced significant changes in ligand-selectivity profiles, the authors assessed these profiles in expressing COS and CHO cell lines using the agonist ligand [125I]IOXY-AGO (5 β -[125Iodo]-3,14-dihydroxy-17-methyl-4-5 α -epoxymorphinan). This ligand's high specific activity (2200 Ci/mmol) and high affinity for μ opioid receptors generated high signal-to-noise ratio binding. The resulting ligand-selectivity profiles of the human and rat μ receptors reveal modest differences in affinities for morphine and naloxone in COS cells but not CHO cells. Ligand-selectivity profiles of the rat and human μ receptors were otherwise similar. Interesting differences between these data and data previously obtained with the peptide agonist [3H]DAMGO suggest that the peptide and alkaloid agonists may label different domains of the μ receptor.

IT 168135-17-9

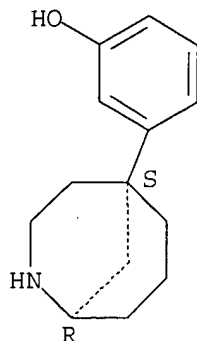
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(cloned human and rat opioid μ -receptor ligand selectivity)

RN 168135-17-9 CAPLUS

CN Phenol, 3-(1R,5S)-2-azabicyclo[3.3.1]non-5-yl- (9CI) (CA INDEX NAME)

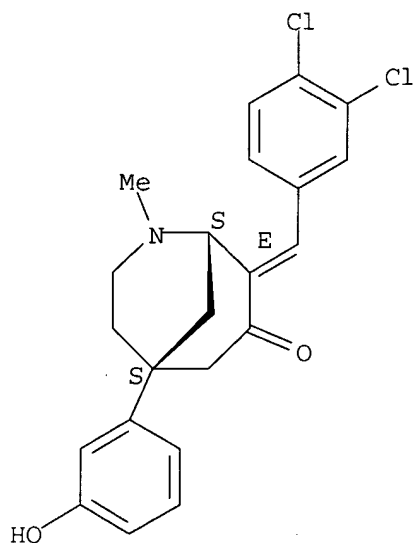
Absolute stereochemistry. Rotation (-).



L6 ANSWER 29 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 1995:596413 CAPLUS
 DOCUMENT NUMBER: 123:75461
 TITLE: CB-64D and CB-184: ligands with high σ_2 receptor affinity and subtype selectivity
 AUTHOR(S): Bowen, Wayne D.; Bertha, Craig M.; Vilner, Bertold J.; Rice, Kenner C.
 CORPORATE SOURCE: Laboratory of Medicinal Chemistry, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, 20892, USA
 SOURCE: European Journal of Pharmacology (1995), 278(3), 257-60
 CODEN: EJPHAZ; ISSN: 0014-2999
 PUBLISHER: Elsevier
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Four members of a novel class of sigma (σ) ligands were investigated for σ subtype selectivity. (-)-1S,5S- and (+)-1R,5R-(E)-8-Benzylidene-5-(3-hydroxyphenyl)-2-methylmorphane-7-one (CB-64L and CB-64D, resp.) exhibited σ_1 K_i = 10.5 nM and 3063 nM; σ_2 K_i = 154 nM and 16.5 nM, resp. The corresponding 3,4-dichloro derivs., (-)-1S,5S- and (+)-1R,5R-(E)-8-(3,4-dichlorobenzylidene)-5-(3-hydroxyphenyl)-2-Me morphane-7-one (CB-182 and CB-184, resp.) were also examined CB-182 ((-)-isomer) showed σ_1 and σ_2 K_i = 27.3 nM and 35.5 nM, resp., whereas CB-184 ((+)-isomer) exhibited σ_1 and σ_2 K_i = 7436 nM and 13.4 nM, resp. Thus, the two σ subtypes showed opposite enantioselectivity for these compds., with (-)>(+) at σ_1 and (+)>(-) at σ_2 . Importantly, CB-64D and CB-184 showed high σ_2 affinity and, resp., 185-fold and 554-fold selectivity for σ_2 receptors over σ_1 . While high σ_2 selectivity relative to σ_1 was achieved with these compds., they both exhibited high affinity at μ (μ) opioid receptors (K_i = 37.6 nM and 4.5 nM, resp.). Despite this, CB-64D and CB-184 will be useful tools for further characterization of σ_2 receptors.
 IT 157752-18-6 157752-20-0 165307-46-0
 165307-47-1
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (CB-64D and CB-184: ligands with high σ_2 receptor affinity and subtype selectivity)
 RN 157752-18-6 CAPLUS
 CN 2-Azabicyclo[3.3.1]nonan-7-one, 5-(3-hydroxyphenyl)-2-methyl-8-(phenylmethylenemorphane)-, (1S,5S,8E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

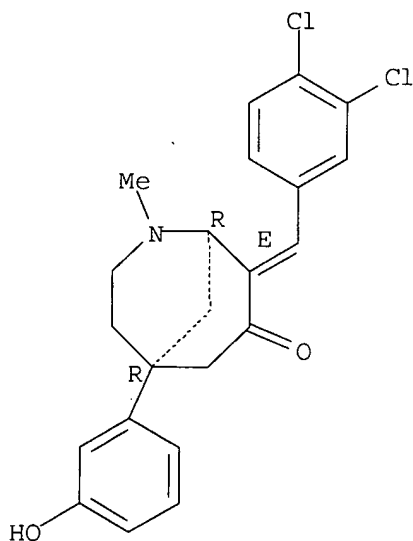
10/762,730



RN 165307-47-1 CAPLUS

CN 2-Azabicyclo[3.3.1]nonan-7-one, 8-[(3,4-dichlorophenyl)methylene]-5-(3-hydroxyphenyl)-2-methyl-, (1R,5R,8E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



L6 ANSWER 30 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

1995:508230 CAPLUS

DOCUMENT NUMBER:

122:230141

TITLE:

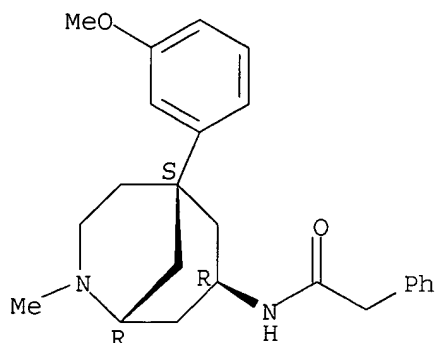
Probes for Narcotic Receptor-Mediated Phenomena. 20.
Alteration of Opioid Receptor Subtype Selectivity of
the 5-(3-Hydroxyphenyl)morphans by Application of the
Message-Address Concept: Preparation of δ -Opioid
Receptor Ligands

AUTHOR(S):

Bertha, Craig M.; Flippen-Anderson, Judith L.;
Rothman, Richard B.; Porreca, Frank; Davis, Peg; Xu,
Heng; Becketts, Karen; Cha, Xian-Yuan; Rice, Kenner C.

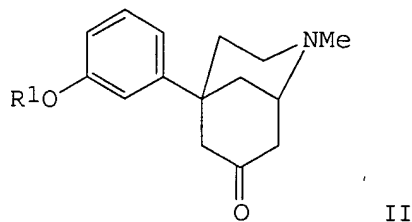
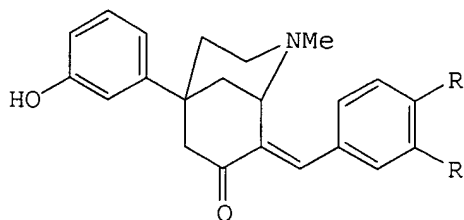
10/762,730

Relative stereochemistry.



● HBr

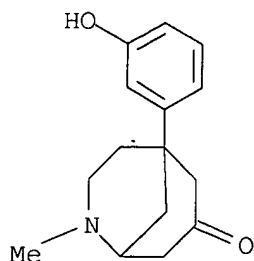
L6 ANSWER 31 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:605756 CAPLUS
DOCUMENT NUMBER: 121:205756
TITLE: A Marked Change of Receptor Affinity of the
2-Methyl-5-(3-hydroxyphenyl)morphans upon Attachment
of an (E)-8-Benzylidene Moiety: Synthesis and
Evaluation of a New Class of σ Receptor Ligands
AUTHOR(S): Bertha, Craig M.; Mattson, Mariena V.;
Flippen-Anderson, Judith L.; Rothman, Richard B.; Xu,
Heng; Cha, Xian-Yuan; Becketts, Karen; Rice, Kenner C.
CORPORATE SOURCE: Laboratory of Medicinal Chemistry, National Institute
of Diabetes and Digestive and Kidney Diseases,
Bethesda, MD, 20892, USA
SOURCE: Journal of Medicinal Chemistry (1994), 37(19), 3163-70
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



AB The (E)-8-benzylidene and (E)-8-(3,4-dichlorobenzylidene), 7-ketone
derivs., I (R = H, Cl), of the synthetic opiate 2-methyl-5-(3-
hydroxyphenyl)morphane [5-(3-hydroxyphenyl)-2-methyl-2-
azabicyclo[3.3.1]nonane], were synthesized from II (R1 = H, Me) via the
Claisen-Schmidt reaction. The corresponding enantiomers of I were
obtained in >99% optical purity from the optical isomers of II (R1 = H),
resolved with the O,O'-dibenzoyltartaric acids. The absolute configurations
of the enantiomers of II (R1 = H) were determined. The determination of the
regioisomer

10/762,730

INDEX NAME)



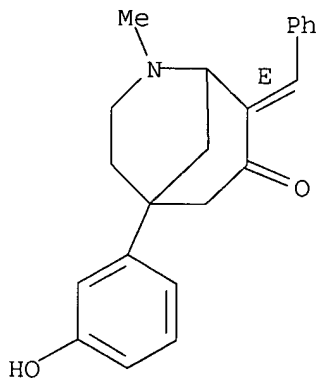
IT 157668-79-6P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation, crystal structure, and opioid binding activity of)

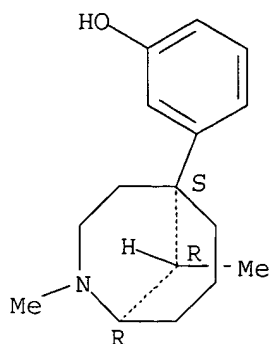
RN 157668-79-6 CAPLUS

CN 2-Azabicyclo[3.3.1]nonan-7-one, 5-(3-hydroxyphenyl)-2-methyl-8-(phenylmethylen)-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L6 ANSWER 32 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:125 CAPLUS
DOCUMENT NUMBER: 120:125
TITLE: Conformational analysis of the opioid phenylmorphane and its 9 α -methyl analog in solution using high-resolution nuclear magnetic resonance spectroscopy
AUTHOR(S): DiMeglio, Christine M.; Froimowitz, Mark; Makriyannis, Alexandros
CORPORATE SOURCE: Sch. Pharm., Univ. Connecticut, Storrs, CT, 06269, USA
SOURCE: Pharmaceutical Research (1993), 10(8), 1200-5
CODEN: PHREEB; ISSN: 0724-8741
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



L6 ANSWER 33 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1993:256 CAPLUS

DOCUMENT NUMBER: 118:256

TITLE: Absolute configuration and conformation of the pure opioid antagonist (+)-2,9α-dimethyl-5-(m-hydroxyphenyl)morphan

AUTHOR(S): Froimowitz, Mark; Pangborn, Walter; Cody, Vivian

CORPORATE SOURCE: Alcohol Drug Res. Cent., McLean Hosp., Belmont, MA, 02178-9106, USA

SOURCE: Chirality (1992), 4(6), 377-83

CODEN: CHRLEP; ISSN: 0899-0042

DOCUMENT TYPE: Journal

LANGUAGE: English

AB (+)-2,9α-Dimethyl-5-(m-hydroxyphenyl)morphan is the only phenylmorphan analog whose affinity for opioid κ-receptors is greater than its affinity for opioid μ-receptors. Pharmacol., the compound is a pure opioid antagonist devoid of agonist activity in in vivo assays of antinociception. The absolute configuration of the compound has been determined to be (1R,5S,9R) from an X-ray crystallog. study of the chloride salt. Thus, the absolute configuration corresponds to that of the atypical opioid agonist (-)-phenylmorphan while the weak atypical agonist (-)-2,9α-dimethyl-5-(m-hydroxyphenyl)morphan corresponds to the potent morphine-like (+)-phenylmorphan. The preferred orientations of the Ph ring for the two stereoisomers were determined using the mol. mechanics program MM2-87 and found to vary from that of the two parent compds. The atypical properties of the two 9α-Me analogs is consistent with an opioid ligand model which proposes that morphine-like properties require a particular range of Ph orientations. There was good agreement between the structure obtained from X-ray crystallog. and computed with the MM2-87 program.

IT 88550-31-6

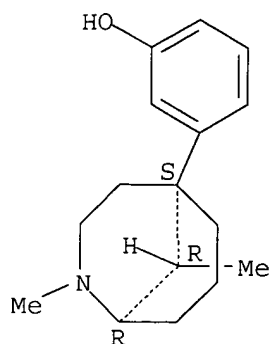
RL: PRP (Properties)

(configuration and conformation of, crystal structure in relation to)

RN 88550-31-6 CAPLUS

CN Phenol, 3-(2,9-dimethyl-2-azabicyclo[3.3.1]non-5-yl)-, hydrochloride, anti-(+)- (9CI) (CA INDEX NAME)

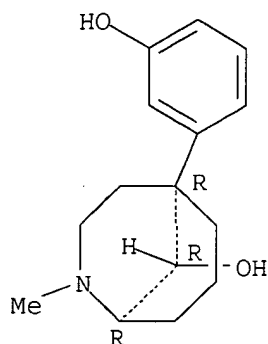
Rotation (+). Absolute stereochemistry unknown.



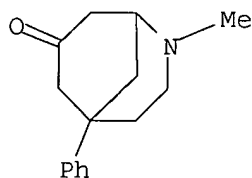
● HCl

L6 ANSWER 34 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
 X ACCESSION NUMBER: 1992:227659 CAPLUS
 DOCUMENT NUMBER: 116:227659
 TITLE: Phenylmorphans and analogs: opioid receptor subtype selectivity and effect of conformation on activity
 AUTHOR(S): Froimowitz, Mark; Pick, Chaim G.; Pasternak, Gavrill W.
 CORPORATE SOURCE: Alcohol Drug Abuse Res. Cent., McLean Hosp., Belmont, MA, 02178, USA
 SOURCE: Journal of Medicinal Chemistry (1992), 35(9), 1521-5
 CODEN: JMCMAR; ISSN: 0022-2623
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The morphine-like (+)-phenylmorphane, the atypical (-)-enantiomer, and some analogs were tested in receptor binding assays selective for opioid μ_1 , μ_2 , δ , κ_1 , and κ_3 receptors. The affinities of all of the compds. except one, including the atypical (-)-phenylmorphane, were greatest for μ_1 and μ_2 receptors. The only exception was the (+)-9 α -Me analog which had slightly greater affinity for the κ_1 receptor. The selective receptor binding assays provide evidence that opioids in which the Ph ring is constrained to be equatorial on the piperidine ring can have considerable affinity for μ receptors. In addition, the analgesic dose-response curves were determined for (+)- and (-)-phenylmorphane using the mouse tail-flick assay with the (+)-enantiomer being 7-fold more potent. Pretreatment with the selective opioid antagonists β -FNA (μ_1 and μ_2), naloxonazine (μ_1), nor-BNI (κ_1), and naltrindole (δ) suggests that the antinociceptive activity of both enantiomers is mediated through μ receptors. The pretreatment with naloxonazine, which attenuated the antinociceptive effect, shows that both (+)- and (-)-phenylmorphans are μ_1 agonists, while intrathecal administration shows that both are μ_2 agonists. Conformational energy calcns. on the compds. were also performed using the MM2-87 program. Consistent with previous conformational results for the phenylmorphans, the most potent antinociceptive compds. preferred a particular orientation of the Ph ring.
 IT 28623-81-6 28623-84-9 88550-29-2
 88550-30-5 88550-32-7 95689-22-8
 95689-26-2
 RL: BIOL (Biological study)
 (analgesic activity and opioid receptor subtype selectivity of)
 RN 28623-81-6 CAPLUS
 CN Phenol, 3-[(1S,5R)-2-methyl-2-azabicyclo[3.3.1]non-5-yl]- (9CI) (CA INDEX NAME)

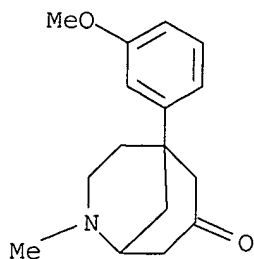
10/762,730



L6 ANSWER 35 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1992:174489 CAPLUS
DOCUMENT NUMBER: 116:174489
TITLE: Carbon-13 NMR chemical shift assignments for
substituted 2-azabicyclo[3.3.1]nonan-7-ones
AUTHOR(S): Casamitjana, Nuria; Bonjoch, Josep; Gracia, Jordi;
Bosch, Joan
CORPORATE SOURCE: Fac. Pharm., Univ. Barcelona, Barcelona, 08028, Spain
SOURCE: Magnetic Resonance in Chemistry (1992), 30(2), 183-5
CODEN: MRCHEG; ISSN: 0749-1581
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The ¹³C NMR spectra of 26 substituted 2-azabicyclo[3.3.1]nonan-7-ones are
reported, providing a diagnostic method for the stereochem. elucidation of
the relative configuration of these products.
IT 140165-64-6 140165-65-7
RL: PRP (Properties)
(carbon-13 NMR of)
RN 140165-64-6 CAPLUS
CN 2-Azabicyclo[3.3.1]nonan-7-one, 2-methyl-5-phenyl- (9CI) (CA INDEX NAME)



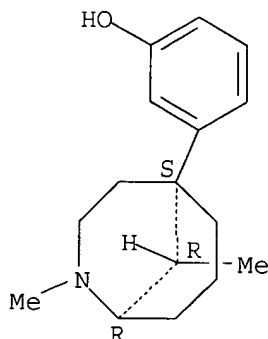
RN 140165-65-7 CAPLUS
CN 2-Azabicyclo[3.3.1]nonan-7-one, 5-(3-methoxyphenyl)-2-methyl- (9CI) (CA
INDEX NAME)



10/762,730

L6 ANSWER 36 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:135894 CAPLUS
DOCUMENT NUMBER: 114:135894
TITLE: Evaluation of new compounds for opioid activity
AUTHOR(S): Woods, J.; Medzihradsky, F.; Smith, C.; Winger, G.;
France, C.
CORPORATE SOURCE: USA
SOURCE: NIDA Research Monograph (1988), 90(Probl. Drug
Depend., 1988), 421-67
CODEN: MIDAD4; ISSN: 0361-8595
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB The opioid activity of different compds. tested in different exptl.
systems are described.
IT **88550-32-7**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); BIOL (Biological study)
(opioid activity of, evaluation of)
RN 88550-32-7 CAPLUS
CN Phenol, 3-(2,9-dimethyl-2-azabicyclo[3.3.1]non-5-yl)-, anti-(-)- (9CI)
(CA INDEX NAME)

Rotation (-). Absolute stereochemistry unknown.



L6 ANSWER 37 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:111859 CAPLUS
Correction of: 1988:486100
DOCUMENT NUMBER: 112:111859
Correction of: 109:86100
TITLE: Biological evaluation of compounds for their physical
dependence potential and abuse liability. X. Drug
testing programs of the Committee on Problems of Drug
Dependence, Inc. (1986)
AUTHOR(S): Jacobson, Arthur E.
CORPORATE SOURCE: Lab. Chem., Natl. Inst. Diabetes Dig. Kidney Dis.,
Bethesda, MD, 20892, USA
SOURCE: NIDA Research Monograph (1987), 76(Probl. Drug
Depend., 1986), 370-91
CODEN: MIDAD4; ISSN: 0361-8595
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A report is given on the drug-testing programs of the Committee on
Problems of Drug Dependence, and new and lit. data are presented from
studies of the dependency potential of a large number of drugs, including
epoxymorphinans, phenylmorphans, benzomorphans, methadone-like compds.,
pethidines, fentanyl, etc.

10/762,730

IT 88550-29-2

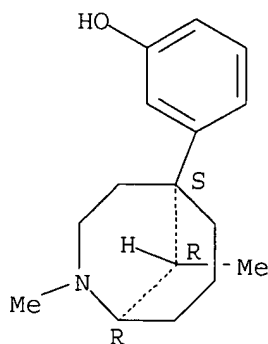
RL: PRP (Properties)

(abuse and dependence potential of)

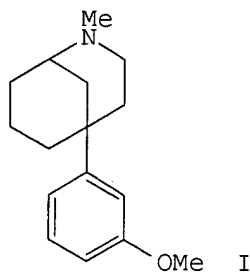
RN 88550-29-2 CAPLUS

CN Phenol, 3-(2,9-dimethyl-2-azabicyclo[3.3.1]non-5-yl)-, anti- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L6 ANSWER 38 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1989:8444 CAPLUS
DOCUMENT NUMBER: 110:8444
TITLE: Functionalized 2-azabicyclo[3.3.1]nonanes. VIII. New synthesis of 5-phenylmorphans
AUTHOR(S): Bonjoch, Josep; Casamitjana, Nuria; Bosch, Joan
CORPORATE SOURCE: Fac. Pharm., Univ. Barcelona, Barcelona, 08028, Spain
SOURCE: Tetrahedron (1988), 44(6), 1735-41
CODEN: TETRAB; ISSN: 0040-4020
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 110:8444
GI



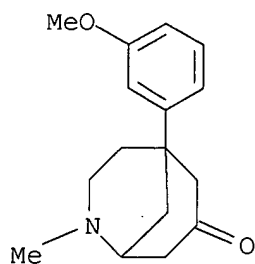
AB A new procedure for the synthesis of 2-azabicyclo[3.3.1]nonanes, e.g. I, by intramol. cyclization of 4-acetonyl-2-piperidinecarbonitriles under acidic conditions is described. The procedure allows the preparation of the pharmacol. interesting 5-phenylmorphans and involves the initial formation of 1-methyl-4-acetonilidenepiperidine, conjugate addition of a diaryl-cuprate, and cyclization of the resulting 4-acetonilpiperidine by way of the corresponding 2-cyano derivative

IT 140165-65-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reduction of)

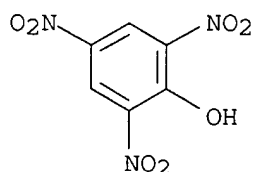
10/762,730

CRN 140165-65-7
CMF C16 H21 N O2

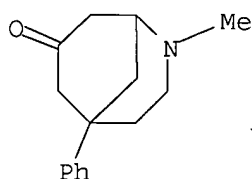


CM 2

CRN 88-89-1
CMF C6 H3 N3 O7



RN 140165-64-6 CAPLUS
CN 2-Azabicyclo[3.3.1]nonan-7-one, 2-methyl-5-phenyl- (9CI) (CA INDEX NAME)



L6 ANSWER 39 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1986:583743 CAPLUS
DOCUMENT NUMBER: 105:183743
TITLE: Evaluation of new compounds for opioid activity (1985)
AUTHOR(S): Woods, James H.; Medzihradsky, Fedor; Smith, Charles B.; Winger, Gail D.; Gmerek, Debra E.
CORPORATE SOURCE: Dep. Pharmacol., Univ. Michigan, Ann Arbor, MI, 48109-0010, USA
SOURCE: NIDA Research Monograph (1986), 67(Probl. Drug Depend.), 453-89
CODEN: MIDAD4; ISSN: 0361-8595
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The opioid-like activity of 36 compds. (benzomorphans, xylidines, morphinans, peptides, phenylpiperazines, etc.) was evaluated and the data were summarized in this report. The test procedures included drug discrimination, dependence liability, and i.v. self-administration in monkeys, displacement of [3H]etorphine from rat cerebral membranes, and inhibition of twitch in elec. driven guinea pig ileum and mouse vas

10/762,730

deferens.

IT 95689-23-9

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(opioid activity of)

RN 95689-23-9 CAPLUS

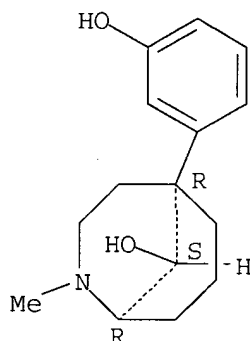
CN Benzeneacetic acid, α -hydroxy-, compd. with syn-5-(3-hydroxyphenyl)-2-methyl-2-azabicyclo[3.3.1]nonan-9-ol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 95689-22-8

CMF C15 H21 N O2

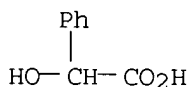
Relative stereochemistry.



CM 2

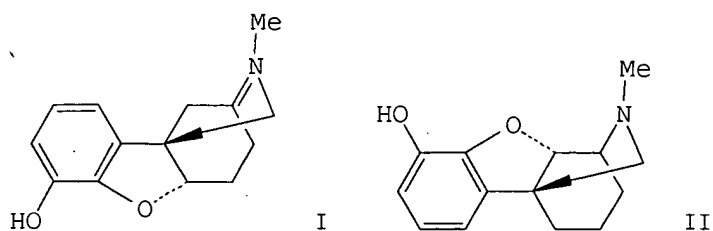
CRN 90-64-2

CMF C8 H8 O3



L6 ANSWER 40 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1985:160031 CAPLUS
DOCUMENT NUMBER: 102:160031
TITLE: Probes for narcotic receptor mediated phenomena 3.
Oxide bridged 5-phenylmorphans
AUTHOR(S): Burke, Terrence R., Jr.; Jacobson, Arthur E.; Rice,
Kenner C.; Weissman, Ben Avi; Silverton, James V.
CORPORATE SOURCE: Lab. Chem., NIH, MD, USA
SOURCE: NIDA Research Monograph (1984), 49, 109-13
CODEN: MIDAD4; ISSN: 0361-8595
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

10/762,730



AB Oxide bridged 5-phenylmorphans (I and II) were prepared and tested for analgesic activity as well as opiate receptor binding properties. The phenylmorphans had no analgesic activity. II exhibited appreciable binding to rat brain homogenate. Structural requirement of the drugs binding to opiate receptors is discussed.

IT **28623-81-6 28623-84-9**

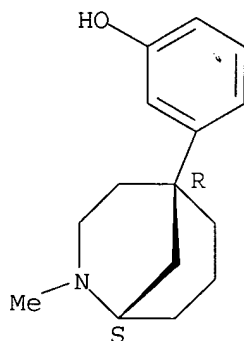
RL: PROC (Process)

(analgesic activity and opiate receptor binding of)

RN 28623-81-6 CAPLUS

CN Phenol, 3-[(1S,5R)-2-methyl-2-azabicyclo[3.3.1]non-5-yl] - (9CI) (CA INDEX NAME)

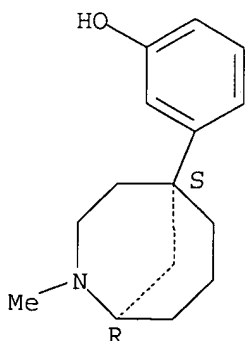
Absolute stereochemistry. Rotation (+).



RN 28623-84-9 CAPLUS

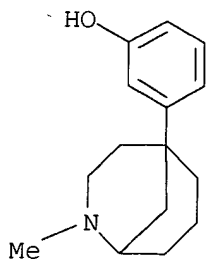
CN Phenol, 3-[(1R,5S)-2-methyl-2-azabicyclo[3.3.1]non-5-yl] - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

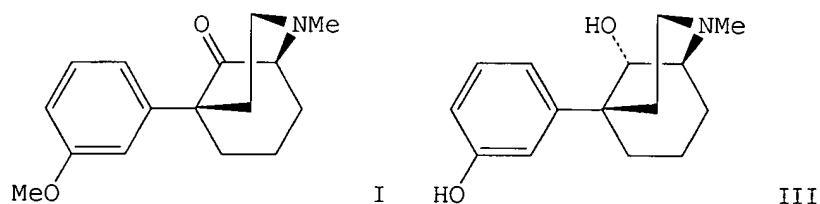


10/762,730

ACCESSION NUMBER: 1985:159988 CAPLUS
DOCUMENT NUMBER: 102:159988
TITLE: Demonstration and affinity labeling of a stereoselective binding site for a benzomorphan opiate on acetylcholine receptor-rich membranes from Torpedo electroplaque
AUTHOR(S): Oswald, Robert E.; Pennow, Nancy N.; McLaughlin, James T.
CORPORATE SOURCE: New York State Coll. Vet. Med., Cornell Univ., Ithaca, NY, 14853, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1985), 82(3), 940-4
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The interaction of an optically pure benzomorphan opiate, (-)-N-allyl-N-normetazocine [(-)-ANMC] [14198-28-8], with the nicotinic acetylcholine receptor from Torpedo electroplaque was studied by using radioligand binding and affinity labeling. The binding was complex with at least 2 specific components having equilibrium dissociation consts. of 0.3 μ M and 2 μ M. The affinity of the higher affinity component was decreased by carbamoylcholine [462-58-8] but not by α -bungarotoxin [11032-79-4]. The effect of carbamoylcholine was not blocked by α -bungarotoxin. In comparison, the affinity of [3H]phencyclidine [77-10-1], a well-characterized ligand for a high-affinity site for noncompetitive blockers on the acetylcholine receptor, is increased by carbamoylcholine and the increase is blocked by α -bungarotoxin. The binding of (-)-[3H]ANMC was inhibited by a number of other benzomorphans, with (-)-isomers being 4- to 5-fold more potent than (+)-isomers. Phencyclidine inhibits the binding of (-)-[3H]ANMC to its high-affinity site by a mechanism that is not competitive. UV-catalyzed affinity labeling indicated that the high-affinity-binding site for (-)-[3H]ANMC is at least partially associated with the δ subunit. Tryptic degradation of the Torpedo marmorata δ chain suggested that (-)-ANMC labeled a 16,000-dalton COOH-terminal portion of the subunit. In contrast, 5-azidotrimethisoquin [75041-53-1], a photoaffinity label of the high-affinity site for noncompetitive blockers, labels a 47,000-dalton NH₂-terminal fragment of the δ subunit. Thus, (-)-[3H]ANMC binds to sites completely distinct from the binding sites for acetylcholine. The high-affinity-binding site for (-)-ANMC and that for phencyclidine and 5-azidotrimethisoquin are allosterically coupled but are regulated differently and are probably phys. distinct.
IT 27107-68-2
RL: BIOL (Biological study)
(normetazocine binding to acetylcholine receptor rich membrane response to, in Torpedo electroplaque)
RN 27107-68-2 CAPLUS
CN Phenol, 3-(2-methyl-2-azabicyclo[3.3.1]non-5-yl)- (9CI) (CA INDEX NAME)



L6 ANSWER 42 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 1985:149088 CAPLUS
 DOCUMENT NUMBER: 102:149088
 TITLE: 9 α - and 9 β -hydroxyphenylmorphans
 AUTHOR(S): Awaya, Hiroyoshi; May, Everette L.; Jacobson, Arthur E.; Aceto, Mario D.
 CORPORATE SOURCE: Med. Coll. Virginia, Virginia Commonw. Univ.,
 Richmond, VA, 23298, USA
 SOURCE: Journal of Pharmaceutical Sciences (1984), 73(12),
 1867-8
 CODEN: JPMSAE; ISSN: 0022-3549
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



AB Platinum oxide hydrogenation of 5-m-methoxyphenyl-2-methyl-9-oxomorphane (I) gave the 9 α -hydroxy racemate whose phenolic analog (II) is a strong antinociceptive agent, fully supportive of morphine dependence in rhesus monkeys. The di-O-acetyl derivative of II was similar to II in its profile of activity. The diastereoisomer of II, obtained by hydrogenation of the methobromide of I, extrusion of Me bromide, and O-demethylation of the resultant free base, was almost inactive antinociceptively and did not suppress withdrawal symptoms in morphine-dependent monkeys. The orientation of the C-9 hydroxyl groups was deduced from spectral data and by analogy.

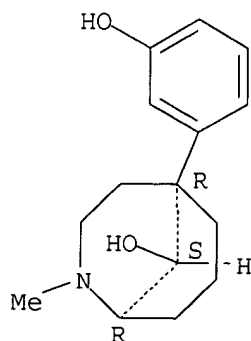
IT 95689-22-8P 95689-23-9P 95689-24-0P
 95689-25-1P 95689-26-2P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation and antinociceptive activity of)

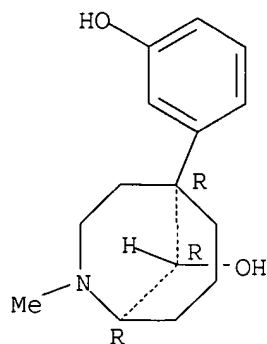
RN 95689-22-8 CAPLUS

CN 2-Azabicyclo[3.3.1]nonan-9-ol, 5-(3-hydroxyphenyl)-2-methyl-, syn- (9CI)
 (CA INDEX NAME)

Relative stereochemistry.

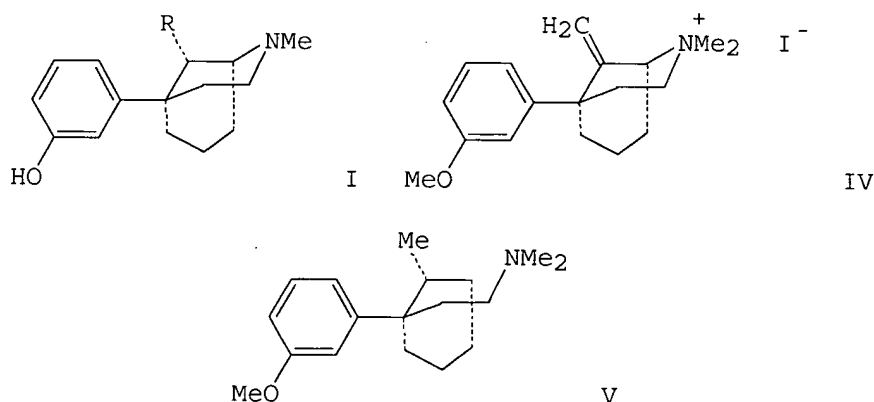


RN 95689-23-9 CAPLUS



● HCl

L6 ANSWER 43 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 1984:121413 CAPLUS
 DOCUMENT NUMBER: 100:121413
 TITLE: Racemic and optically active 2,9-dimethyl-5-(m-hydroxyphenyl)morphans and pharmacological comparison with the 9-demethyl homologs
 AUTHOR(S): Awaya, Hiroyoshi; May, Everette L.; Aceto, Mario D.; Merz, Herbert; Rogers, Michael E.; Harris, Louis S.
 CORPORATE SOURCE: Dep. Pharmacol., Med. Coll. Virginia, Richmond, VA, 23298, USA
 SOURCE: Journal of Medicinal Chemistry (1984), 27(4), 536-9
 CODEN: JMCMAR; ISSN: 0022-2623
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



AB Dimethyl(hydroxyphenyl)morphane I (R = Me) (II) was prepared from 5-(m-methoxyphenyl)-2-methyl-9-oxomorphane and resolved into its enantiomers. The α -orientation of the C-9 Me group was derived from studies of induced NMR shifts. (+)-II has inappreciable agonist (antinociceptive) activity in mice, and (-)-II shows codeine-like potency in the hot-plate and writhing tests only. The 9-demethyl homologs I (R = H) (III) are strong agonists, about as potent as morphine in these tests as well as in the tail-flick assay. (\pm)-II and (+)-II, but not (-)-I,

10/762,730

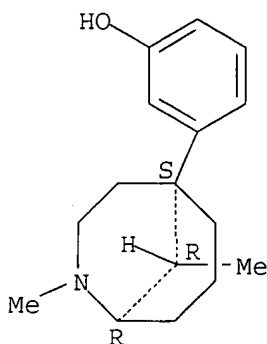
IT 88550-33-8P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 88550-33-8 CAPLUS

CN Phenol, 3-(2,9-dimethyl-2-azabicyclo[3.3.1]non-5-yl)-, hydrochloride,
anti-(-)- (9CI) (CA INDEX NAME)

Rotation (-). Absolute stereochemistry unknown.



● HCl

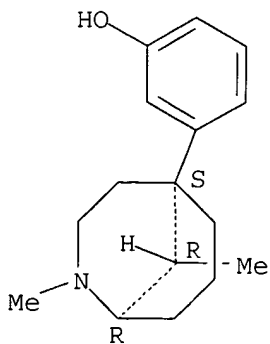
IT 88550-29-2P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation, resolution, and narcotic antagonist and agonist activities of)

RN 88550-29-2 CAPLUS

CN Phenol, 3-(2,9-dimethyl-2-azabicyclo[3.3.1]non-5-yl)-, anti- (9CI) (CA
INDEX NAME)

Relative stereochemistry.



L6 ANSWER 44 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1983:27684 CAPLUS

DOCUMENT NUMBER: 98:27684

TITLE: Biological evaluation of compounds for their
dependence liability. V. Drug testing program of the
Committee on Problems of Drug Dependence, Inc. (1981)

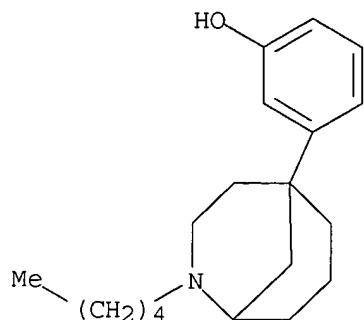
AUTHOR(S): Jacobson, A. E.

CORPORATE SOURCE: Lab. Chem., Natl. Inst. Arthritis, Diabetes Dig.

Kidney Dis., Bethesda, MD, 20205, USA

SOURCE: NIDA Research Monograph (1982), Volume Date 1981, 41,
331-7

10/762,730

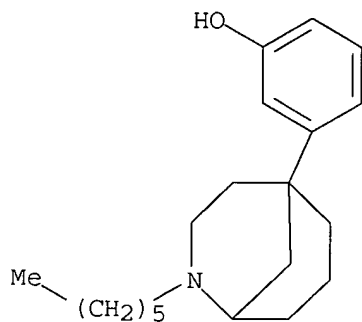


● HCl

RN 83502-18-5 CAPLUS

CN Phenol, 3-(2-hexyl-2-azabicyclo[3.3.1]non-5-yl)-, hydrochloride, (+)-
(9CI) (CA INDEX NAME)

Rotation (+).



● HCl

L6 ANSWER 45 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1982:592941 CAPLUS

DOCUMENT NUMBER: 97:192941

TITLE: Dependence studies of new compounds in the rhesus monkey, rat, and mouse (1981)

AUTHOR(S): Aceto, M. D.; Harris, L. S.; May, E. L.

CORPORATE SOURCE: Med. Coll. Virginia, Virginia Commonw. Univ.,
Richmond, VA, 23298, USA

SOURCE: NIDA Research Monograph (1982), Volume Date 1981, 41,
338-80

CODEN: MIDAD4; ISSN: 0361-8595

DOCUMENT TYPE: Journal

LANGUAGE: English

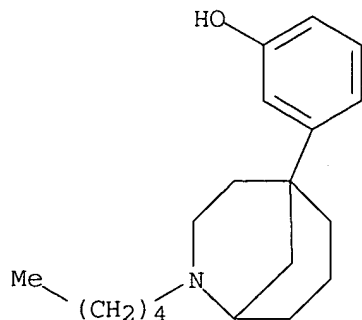
AB Sixty-six compds. were tested for dependence in the rhesus monkey, rat,
and mouse by various methods.

IT 27107-49-9 27107-50-2 83502-15-2

83502-16-3 83502-17-4 83502-18-5

RL: BIOL (Biological study)

10/762,730

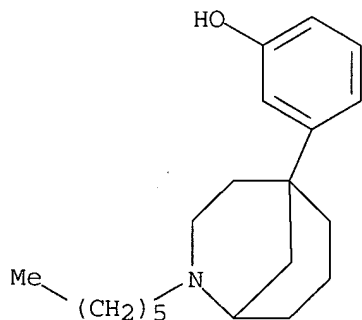


● HCl

RN 83502-18-5 CAPLUS

CN Phenol, 3-(2-hexyl-2-azabicyclo[3.3.1]non-5-yl)-, hydrochloride, (+)-
(9CI) (CA INDEX NAME)

Rotation (+).



● HCl

L6 ANSWER 46 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1982:555939 CAPLUS

DOCUMENT NUMBER: 97:155939

TITLE: Structural requirements for affinity and intrinsic activity at the opiate receptor defined in 4-phenylpiperidine and related series

AUTHOR(S): Zimmerman, D. M.; Smits, S. E.; Hynes, M. D.; Cantrell, B. E.; Reamer, M.; Nickander, R.

CORPORATE SOURCE: Lilly Res. Lab., Eli Lilly and Co., Indianapolis, IN, 46285, USA

SOURCE: NIDA Research Monograph (1982), Volume Date 1981, 41, 112-18

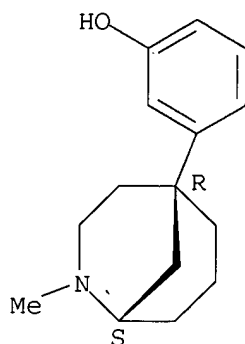
CODEN: MIDAD4; ISSN: 0361-8595

DOCUMENT TYPE: Journal

LANGUAGE: English

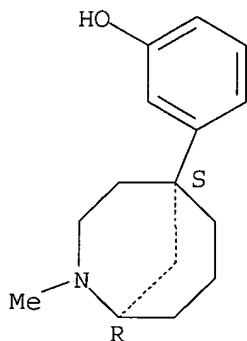
GI

10/762,730



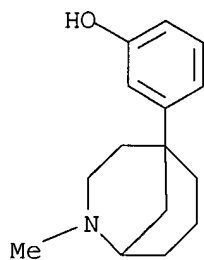
RN 28623-84-9 CAPLUS
CN Phenol, 3-[(1R,5S)-2-methyl-2-azabicyclo[3.3.1]non-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L6 ANSWER 47 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1981:604248 CAPLUS
DOCUMENT NUMBER: 95:204248
TITLE: Phenylpropylamino groups of morphine analgesics plotted with a computer
AUTHOR(S): Brouant, P.; Soyfer, J. C.
CORPORATE SOURCE: Lab. Pharm. Chim., Fac. Pharm., Marseille, F 13385/5, Fr.
SOURCE: Annales Pharmaceutiques Francaises (1981), 39(2), 125-31
CODEN: APFRAD; ISSN: 0003-4509
DOCUMENT TYPE: Journal
LANGUAGE: French
AB The conformational variations of the phenylpropylamino group of morphine and related analgesics were plotted with a computer on the basis of crystallog. data. The analgesic activity was related to the conformational variations.
IT **76580-81-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(conformation of phenylpropylamino group in, computer-plotted, analgesic activity in relation to)
RN 76580-81-9 CAPLUS
CN Phenol, 3-(2-methyl-2-azabicyclo[3.3.1]non-5-yl)-, hydrobromide (9CI) (CA INDEX NAME)

10/762,730



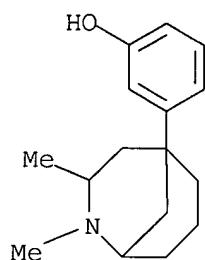
● HBr

56 ANSWER 48 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1981:83962 CAPLUS
DOCUMENT NUMBER: 94:83962
TITLE: Phenylmorphane derivatives
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Jpn. Kokai Tokkyo Koho, 19 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 55124768	A2	19800926	JP 1980-32566	19800311
FR 2451368	A1	19801010	FR 1980-5179	19800307
FR 2451368	B1	19830318		
BE 882152	A1	19800910	BE 1980-9743	19800310
HU 22162	O	19820428	HU 1980-561	19800310
HU 179836	B	19821228		
CA 1148150	A1	19830614	CA 1980-347364	19800310
EP 18077	A2	19801029	EP 1980-300746	19800311
EP 18077	A3	19801126		
R: DE, GB, NL, SE				
GB 2045248	A	19801029	GB 1980-8172	19800311
GB 2045248	B2	19830505		
EP 59989	A1	19820915	EP 1982-102714	19800311
R: DE, GB, NL, SE				
US 4278797	A	19810714	US 1980-150763	19800519
GB 2111976	A1	19830713	GB 1982-27192	19820923
PRIORITY APPLN. INFO.:			US 1979-19527	A 19790312
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			GB 1980-8172	A3 19800311
OTHER SOURCE(S):			CASREACT 94:83962	
GI				

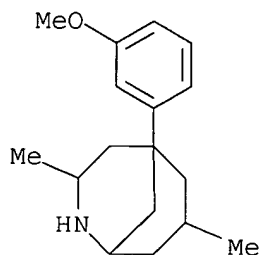
10/762,730



● HBr

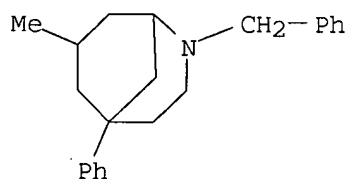
RN 76580-91-1 CAPLUS

CN 2-Azabicyclo[3.3.1]nonane, 5-(3-methoxyphenyl)-3,7-dimethyl- (9CI) (CA INDEX NAME)



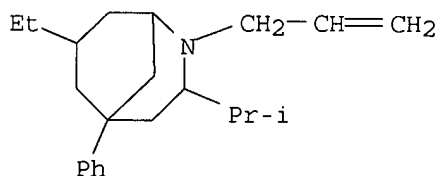
RN 76580-92-2 CAPLUS

CN 2-Azabicyclo[3.3.1]nonane, 7-methyl-5-phenyl-2-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 76580-93-3 CAPLUS

CN 2-Azabicyclo[3.3.1]nonane, 7-ethyl-3-(1-methylethyl)-5-phenyl-2-(2-propenyl)- (9CI) (CA INDEX NAME)



10/762,730

TITLE: Application of metalated enamines to alkaloid synthesis. An expedient approach to the synthesis of morphine-based analgesics

AUTHOR(S): Evans, D. A.; Mitch, C. H.; Thomas, R. C.; Zimmerman, D. M.; Robey, R. L.

CORPORATE SOURCE: Dep. Chem., California Inst. Technol., Pasadena, CA, 91125, USA

SOURCE: Journal of the American Chemical Society (1980), 102(18), 5955-6
CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE: Journal

LANGUAGE: English

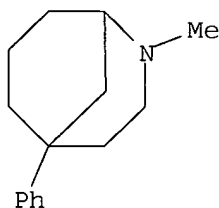
GI For diagram(s), see printed CA Issue.

AB Catalytic hydrogenation of the phenylpiperidine I (R = CH₂CH:CH₂), obtained by treatment of 1-methyl-4-phenyl-1,2,4,5-tetrahydropyridine with BuLi followed by H₂C:CHCH₂Br, gave the piperidine II. I (R = CH₂CH:CH₂) was treated with H₃PO₄-HCO₂H to give the cyclic enamine, which was hydrogenated to give the phenylmorphinan III. I [R = (CH₂)₄Cl] was cyclized with Na I to give the octahydroisoquinoline IV, which hydrogenated to give the corresponding cis- or trans-decahydroisoquinoline depending on hydrogenation conditions. IV was treated with ethereal perchloric acid to give the trans fused immonium perchlorate which was converted to the morphinan V.

IT **74904-15-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 74904-15-7 CAPLUS

CN 2-Azabicyclo[3.3.1]nonane, 2-methyl-5-phenyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

L6 ANSWER 50 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1980:532662 CAPLUS

DOCUMENT NUMBER: 93:132662

TITLE: Radiocrystallographic study of variations in skeletal conformation in morphine analgesics

AUTHOR(S): Brouant, P.; Soyfer, J. C.

CORPORATE SOURCE: Lab. Pharm. Chim., Fac. Pharm., Marseille, 13385/4, Fr.

SOURCE: Annales Pharmaceutiques Francaises (1979), 37(9-10); 461-8

CODEN: APFRAD; ISSN: 0003-4509

DOCUMENT TYPE: Journal

LANGUAGE: French

AB Eight parameters, defined from the crystallog. coordinates, for 21 analgesics containing the phenylpropylamine group, were based on the distance between the N atom and a quaternary C atom center, various planes or centers in aromatic rings. The distances formed 4 distinct sets which were

10/762,730

related to their physiol. activity. The conformations of the morphine-like analgesics was discussed.

IT 53467-24-6

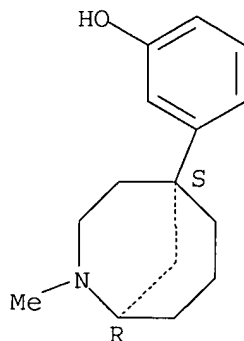
RL: RCT (Reactant); RACT (Reactant or reagent)

(conformation and crystal and mol. structure of, analgesic activity in)

RN 53467-24-6 CAPLUS

CN Phenol, 3-(2-methyl-2-azabicyclo[3.3.1]non-5-yl)-, hydrobromide, (1R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



● HBr

L6 ANSWER 51 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1977:50482 CAPLUS

DOCUMENT NUMBER: 86:50482

TITLE: Azabicycloalkanes as analgetics. 3.
Structure-activity relations of 1-phenyl-6-azabicyclo[3.2.1]octanes and absolute stereochemistry of (+)-1-(3-hydroxyphenyl)-6-methyl-6-azabicyclo[3.2.1]octane and its 7-endo-methyl derivative

AUTHOR(S): Takeda, Mikio; Inoue, Hirozumi; Noguchi, Katsuyuki; Honma, Yasushi; Kawamori, Masatoshi; Tsukamoto, Goro; Yamawaki, Yasuhiko; Saito, Seiichi; Aoe, Keiichi; et al.

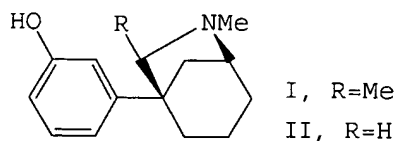
CORPORATE SOURCE: Res. Lab., Tanabe Seiyaku Co. Ltd., Japan
SOURCE: Journal of Medicinal Chemistry (1977), 20(2), 221-8
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

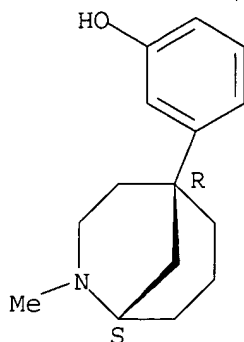
OTHER SOURCE(S): CASREACT 86:50482

GI



AB A series of 53 1-phenyl-6-azabicyclo[3.2.1]octanes was tested for analgesic and narcotic antagonist activities and structure-activity

10/762,730

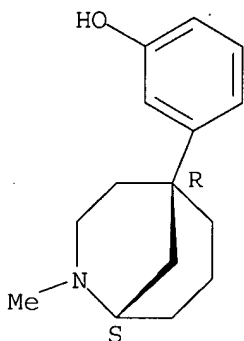


● HCl

RN 28623-81-6 CAPLUS

CN Phenol, 3-[(1S,5R)-2-methyl-2-azabicyclo[3.3.1]non-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L6 ANSWER 52 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1975:51660 CAPLUS

DOCUMENT NUMBER: 82:51660

TITLE: Improved synthesis and additional pharmacology of the potent analgetic (-)-5-m-hydroxyphenyl-2-methylmorphane

AUTHOR(S): Rogers, Michael E.; May, Everette L.

CORPORATE SOURCE: Natl. Inst. Arthritis, Metab. Dig. Dis., Natl. Inst. Health, Bethesda, MD, USA

SOURCE: Journal of Medicinal Chemistry (1974), 17(12), 1328-30
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

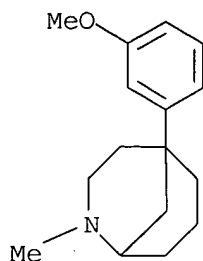
LANGUAGE: English

GI For diagram(s), see printed CA Issue.

AB The title compound (I) [27107-68-2] (16 mg/kg/day s.c.) produced very slight phys. dependence in Rhesus monkeys. Nalorphine and naloxone did not precipitate withdrawal symptoms in monkeys receiving I. At 32 mg/kg, I produced convulsions in monkeys. The 24-hr LD50 of I in mice was 137 mg/kg s.c. The yield of I in the previously reported synthesis (E. L. May and J. G. Murphy, 1955) was improved by changing the conditions for dimethylaminoethylation of 2-m-methoxyphenylcyclohexanone (II) [15547-89-4] and improving the resolution procedure. An alternative synthesis of I was described in which II was alkylated with Et

10/762,730

(9CI) (CA INDEX NAME)



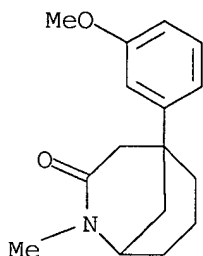
● HBr

IT 53661-48-6

RL: RCT (Reactant); RACT (Reactant or reagent)
(reduction of)

RN 53661-48-6 CAPLUS

CN 2-Azabicyclo[3.3.1]nonan-3-one, 5-(3-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)



L6 ANSWER 53 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1975:25673 CAPLUS

DOCUMENT NUMBER: 82:25673

TITLE: Stereochemistry and absolute configuration of the
analgesic agonist-antagonist (-)-5-m-hydroxyphenyl-2-
methyilmorphan

AUTHOR(S): Cochran, Todd G.

CORPORATE SOURCE: Sch. Pharm., Duquesne Univ., Pittsburgh, PA, USA

SOURCE: Journal of Medicinal Chemistry (1974), 17(9), 987-9
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

GI For diagram(s), see printed CA Issue.

AB Addnl. data considered in abstracting and indexing are available from a
source cited in the original document. The absolute configuration of
(-)-5-m-hydroxyphenyl-2-methyilmorphan-HBr (I-HBr) [53467-24-6]
was established as 1R, 5S by single-crystal x-ray anal. Both rings of the
azabicyclononane system exist in chair conformations with the Ph and Me
substituents equatorial. The distance between the cationic N and the
aromatic ring is 5.66 Å. The relation between conformation and activity
and receptor interaction was discussed.

IT 53467-24-6

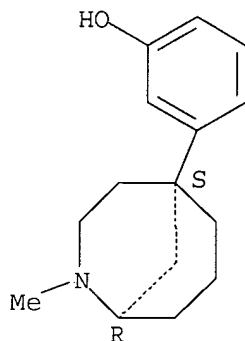
RL: PRP (Properties)
(absolute configuration of)

10/762,730

RN 53467-24-6 CAPLUS

CN Phenol, 3-(2-methyl-2-azabicyclo[3.3.1]non-5-yl)-, hydrobromide, (1R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



● HBr

L6 ANSWER 54 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1974:91126 CAPLUS

DOCUMENT NUMBER: 80:91126

TITLE: Phenylmorphane agonists-antagonists

AUTHOR(S): Ong, Helen H.; Ohishi, Tokuro; May, Everette L.

CORPORATE SOURCE: Natl. Inst. Arthritis, Metab. Dig. Dis., Natl. Inst. Health, Bethesda, MD, USA

SOURCE: Journal of Medicinal Chemistry (1974), 17(1), 133-4
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

AB (+)-5-(M-hydroxyphenyl)-2-propylmorphane-HBr (I) [51264-07-4], (+)-2-allyl-5-(m-hydroxyphenyl)morphane-HBr (II) [51264-08-5], and (+)-2-(cyclopropylmethyl)-5-(m-hydroxyphenyl)morphane-HBr (III) [51264-09-6] and the corresponding racemates were prepared and tested as analgesics. I and II were prepared by alkylation of (+)-5-(m-hydroxyphenyl)morphane (IV) [51264-10-9], while III was prepared by acylation of IV, followed by LiAlH₄ reduction. The analgesic activities of I, II, and III were 2-3 times higher than the corresponding racemates in the Nilsen test. With the hot plate test, I was 3 times more potent than its racemate. Analgesic and antagonist activities of the phenylmorphane derivative isomers were related to nalorphine-HCl [57-29-4], pentazocine-HCl [2276-52-0], and morphine sulfate [64-31-3].

IT 51596-46-4 51596-47-5

RL: RCT (Reactant); RACT (Reactant or reagent)
(demethylation of)

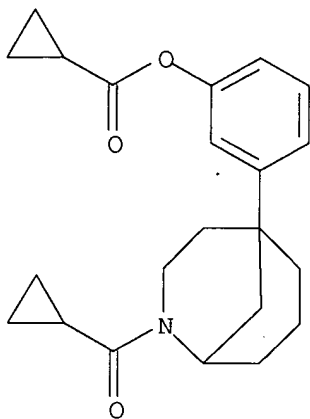
RN 51596-46-4 CAPLUS

CN 2-Azabicyclo[3.3.1]nonane, 5-(3-methoxyphenyl)-, hydrobromide (9CI) (CA INDEX NAME)

10/762,730

RN 51596-51-1 CAPLUS

CN Cyclopropanecarboxylic acid, 3-[2-(cyclopropylcarbonyl)-2-azabicyclo[3.3.1]non-5-yl]phenyl ester (9CI) (CA INDEX NAME)



L6 ANSWER 55 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1972:140587 CAPLUS

DOCUMENT NUMBER: 76:140587

TITLE: Photocyclizations. II. Synthesis of iminoethanophenanthridine (seven-membered ring) homologs

AUTHOR(S): Ong, Helen H.; May, Everette L.

CORPORATE SOURCE: Natl. Inst. Arthritis Metab. Dis., Natl. Inst. Health, Bethesda, MD, USA

SOURCE: Journal of Organic Chemistry (1972), 37(5), 712-16
CODEN: JOCEAH; ISSN: 0022-3263

DOCUMENT TYPE: Journal

LANGUAGE: English

GI For diagram(s), see printed CA Issue.

AB Photolysis of 9-cis-chloroacetamino-5-(m-hydroxyphenyl)-2-methyl-2-azabicyclo[3.3.1]nonane gave both ortho and para ring closure to propanopyridobenzazepinones (I and II) whose structures were deduced from mass and NMR spectral data and by chemical evidence.

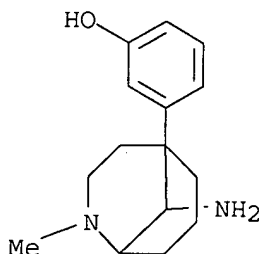
IT **32969-96-3P 32969-97-4P 32969-98-5P**

33068-03-0P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 32969-96-3 CAPLUS

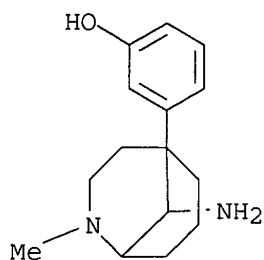
CN Phenol, 3-(9-amino-2-methyl-2-azabicyclo[3.3.1]non-5-yl)- (9CI) (CA INDEX NAME)



RN 32969-97-4 CAPLUS

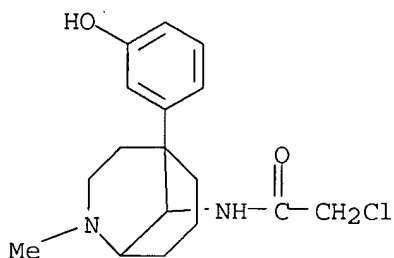
10/762,730

CN Phenol, 3-(9-amino-2-methyl-2-azabicyclo[3.3.1]non-5-yl)-, dihydrobromide
(9CI) (CA INDEX NAME)

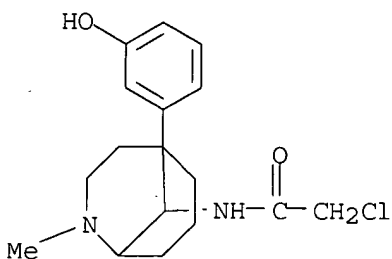


● 2 HBr

RN 32969-98-5 CAPLUS
CN Acetamide, 2-chloro-N-[5-(3-hydroxyphenyl)-2-methyl-2-azabicyclo[3.3.1]non-9-yl]- (9CI) (CA INDEX NAME)



RN 33068-03-0 CAPLUS
CN Acetamide, 2-chloro-N-[5-(3-hydroxyphenyl)-2-methyl-2-azabicyclo[3.3.1]non-9-yl]-, monohydrochloride (9CI) (CA INDEX NAME)



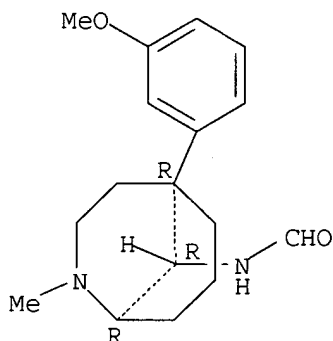
● HCl

L6 ANSWER 56 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1972:85730 CAPLUS
DOCUMENT NUMBER: 76:85730
TITLE: Iminoethanophenanthridines by the Pictet-Spengler reaction
AUTHOR(S): Ong, Helen H.; May, Everette L.

10/762,730

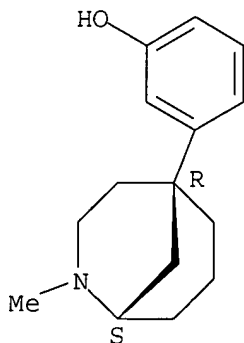
CORPORATE SOURCE: Natl. Inst. Arthritis Metab. Dis., Natl. Inst. Health, Bethesda, MD, USA
SOURCE: Journal of Heterocyclic Chemistry (1971), 8(6), 1007-9
CODEN: JHTCAD; ISSN: 0022-152X
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB Pictet-Spengler cyclization of 9-cis-amino-5-(m-methoxyphenyl)-2-methyl-2-azabicyclo[3.3.1]nonane (I) gave 2,3,4,4a,5,6-hexahydro-9-methoxy-3-methyl-1H-4,10b-propanobenzo[c][1,7]naphthyridine (II), derivs. of which were weakly analgesic. Thus, I was refluxed 4 hr in EtOH-HCHO-HCl to give 82% II. 2HCl, which was converted to the O-demethyl derivative (III) with HBr. III was treated with cyclopropylcarbonyl chloride-Et3N and the product reduced with LiAlH4 to give the 5-(cyclopropylmethyl) derivative (IV) of III. The hot-plate test showed that III and IV possessed .apprx.14% the analgesic activity of codeine.
IT **35190-80-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 35190-80-8 CAPLUS
CN Formamide, N-[5-(3-methoxyphenyl)-2-methyl-2-azabicyclo[3.3.1]non-9-yl]-, anti- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L6 ANSWER 57 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1970:487772 CAPLUS
DOCUMENT NUMBER: 73:87772
TITLE: Optical isomers of miscellaneous strong analgetics
AUTHOR(S): May, Everette L.; Takeda, Mikio
CORPORATE SOURCE: Nat. Inst. of Arthritis and Metab. Dis., Nat. Inst. of Health, Bethesda, MD, USA
SOURCE: Journal of Medicinal Chemistry (1970), 13(5), 805-7
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB Optical isomers of α -5,9-diethyl-2'-methoxy- (Ia), α -2,5-dimethyl-9-ethyl-2'-hydroxy- (Id), and 2'-hydroxy-2-methyl-6,7-benzomorphans (Ic) and of 5-(m-hydroxyphenyl)-2-methylmorphane (II) have been prepared and compared with parent racemates in analgetic activity, physical dependence capacity, and antagonistic behavior. Racemate Ic, (+)-Ic, (-)-Ic and (-)-II, have morphine-like analgetic and nalorphine-like antagonistic action. Ia was prepared from Ib.
IT **27107-49-9P 27107-50-2P 28623-81-6P**
28623-84-9P 31798-03-5P
RL: SPN (Synthetic preparation); PREP (Preparation)

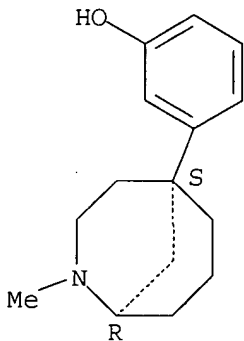
10/762,730



RN 28623-84-9 CAPLUS

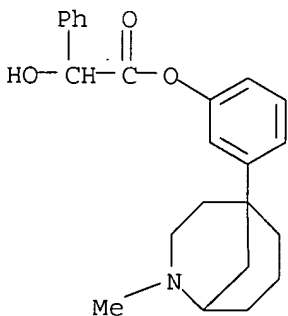
CN Phenol, 3-[(1R,5S)-2-methyl-2-azabicyclo[3.3.1]non-5-yl] - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 31798-03-5 CAPLUS

CN Mandelic acid, (+)-m-(2-methyl-2-azabicyclo[3.3.1]non-5-yl)phenyl ester, D- (8CI) (CA INDEX NAME)



L6 ANSWER 58 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1959:122365 CAPLUS

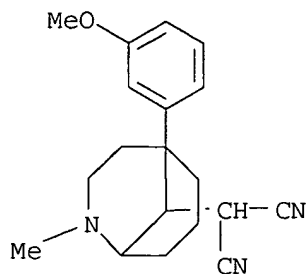
DOCUMENT NUMBER: 53:122365

ORIGINAL REFERENCE NO.: 53:22043e-i

TITLE: Structures related to morphine. X. A position isomer of (+)-3-hydroxy-N-methylmorphinan (Racemorphan)

AUTHOR(S): May, Everett L.

CORPORATE SOURCE: Natl. Inst. of Arthritis and Metabolic Diseases,



● HCl

L6 ANSWER 59 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1958:11165 CAPLUS

DOCUMENT NUMBER: 52:11165

ORIGINAL REFERENCE NO.: 52:2032d-i

TITLE: Structures related to morphine. VI. N-Phenylethyl derivatives of some phenyl- and benzomorphans

AUTHOR(S): May, Everette L.

CORPORATE SOURCE: Natl. Insts. of Health, Bethesda, MD

SOURCE: Journal of Organic Chemistry (1956), 21, 899-901

CODEN: JOCEAH; ISSN: 0022-3263

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

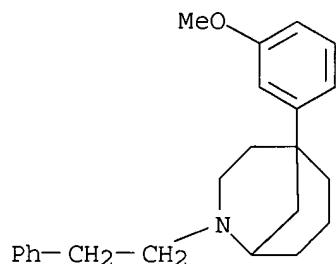
AB cf. C.A. 50, 15560h. N-Me derivs. were converted to N-phenylethyl analogs. These were shown two to three times less effective than the respective N-Me counterparts in producing analgesia in mice, contrary to results obtained with meperidine and race-morphan types. To 1.2 g. BrCN in 7 ml. dry CHCl₃ was added 2.4 g. 5-(m-methoxyphenyl)-2-methylmorphan (I) in 10 ml. CHCl₃ during 45 min. while stirring, refluxed 3 hrs., evaporated to dryness in vacuo, the residue dissolved in EtOH, refluxed briefly, evaporated to dryness, 10 ml. EtOAc added to recover 0.5 g. I.HBr, m. 158-62°. Filtrate freed from EtOAc in vacuo, the residue and 45 ml. 6% HCl refluxed overnight, cooled to 0°, basified with 10% KOH, the liberated oil dried in ether, 32% HBr-AcOH added, kept overnight at 0°, the semisolid washed with ether, and triturated with EtOAc containing a little acetone gave 1.3 g. 2-(m-methoxyphenyl)morphan-HBr (II), m. 127-30°, 67% yield (with 0.3 g. from filtrate), m. 129-31° (acetone-ether); picrate, yellow prisms, m. 162-5° (EtOH). Phenylacetyl chloride (1.0 ml.) added during 3-5 min. to a stirred mixture of 1.0 g. II, 1.5 g. K₂CO₃, 5 ml. H₂O, and 15 ml. MeOH, stirred 1 hr., diluted with 3 volume H₂O, extracted with ether, the extract washed

with dilute HCl and dilute NaOH, dried, and evaporated to dryness gave 1.5 g. sirup, which in 20 ml. dry ether treated gradually with 20 ml. 1.4M ethereal LiAlH₄, refluxed overnight, treated carefully with 10-15 ml. H₂O, the ether decanted from residual hydroxides which were washed three times, combined ether portions dried, and acidified with 32% HBr-AcOH gave 1.1 g. 5-(m-methoxyphenyl)-2-(2-phenylethyl)morphan-HBr (III), leaflets, m. 209-11° (acetone). III (1.1 g.) refluxed in 7 ml. 48% HBr 30 min., evaporated to dryness, and the residue triturated with absolute EtOH containing a

little acetone gave 0.8 g. 5-(m-hydroxyphenyl)-2-(2-phenylethyl)morphan-HBr, m. 274-7.5° (from MeOH). To 0.5 g. BrCN in 3 ml. CHCl₃ was added 0.9 g. 5-phenyl-2-methyl-morphan in 5 ml. CHCl₃ during 1 hr., refluxed 3 hrs., evaporated to dryness, dissolved in a little EtOH, refluxed

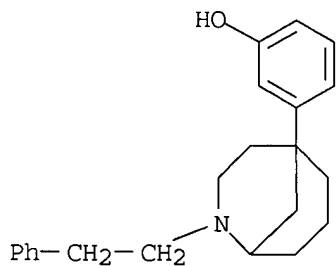
briefly, evaporated to dryness, and the residual sirup with 20 ml. 6% HCl refluxed overnight gave an almost clear solution which was shaken with ether, the aqueous layer basified with 10% NaOH, the oil in ether dried and brought to reaction with phenylacetyl chloride as described above. The resultant amide (1.3 g.) reduced with 15 ml. 1.4M ethereal LiAlH₄ gave 0.8 g. 5-phenyl-2-(2-phenylethyl)morphan-HBr, glittering plates, m. 264-7° (EtOH); picrate, yellow cubes, m. 184-6° (acetone-EtOH). By the same way, 1.6 g. 2,5-dimethyl-6,7-benzomorphan yielded 1.1 g. 5-methyl-2-(2-phenylethyl)-6,7-benzomorphan-HCl, m. 278-80° (decomposition) (absolute EtOH); picrate, m. 142-6° (EtOH).

IT **114279-13-9**, 2-Azabicyclo[3.3.1]nonane, 5-(m-methoxyphenyl)-2-phenethyl-, hydrobromide **114353-67-2**, 2-Azabicyclo[3.3.1]nonane, 5-(m-hydroxyphenyl)-2-phenethyl-, hydrobromide (preparation of)
 RN 114279-13-9 CAPLUS
 CN 2-Azabicyclo[3.3.1]nonane, 5-(m-methoxyphenyl)-2-phenethyl-, hydrobromide (6CI) (CA INDEX NAME)



● HBr

RN 114353-67-2 CAPLUS
 CN Phenol, m-2-phenethyl-2-azabicyclo[3.3.1]non-5-yl-, hydrobromide (6CI) (CA INDEX NAME)



● HBr

L6 ANSWER 60 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 1956:44580 CAPLUS
 DOCUMENT NUMBER: 50:44580
 ORIGINAL REFERENCE NO.: 50:8635d-i,8636a
 TITLE: Structures related to morphine. IV. m-Substituted phenylcyclohexane derivatives
 AUTHOR(S): May, Everette L.; Murphy, James G.

CORPORATE SOURCE: Natl. Inst. of Health, Bethesda, MD
 SOURCE: Journal of Organic Chemistry (1955), 20, 1197-1201
 CODEN: JOCEAH; ISSN: 0022-3263

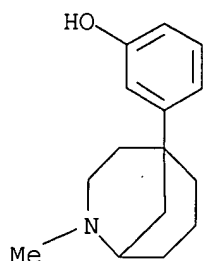
DOCUMENT TYPE: Journal
 LANGUAGE: Unavailable
 OTHER SOURCE(S): CASREACT 50:44580

AB cf. C.A. 50, 4165a. 1-(2-Dimethylaminoethyl)-1-(m-hydroxyphenyl)cyclohexane (I) and 5-(m-hydroxyphenyl)-2-methylmorphane (II) have been prepared to be tested for their analgesic activity. Stirring 14 g. 2-(m-methoxyphenyl)-1-nitro-4-cyclohexene in 105 cc. 95% EtOH 1 h. in a N atmospheric with 90 cc. alc. NaOEt (from 3 g. Na), then adding (40 min.) 240 cc. H₂O, 180 cc. 95% EtOH, and 72 cc. concentrated HCl at -5° to 0° with stirring, stirring the mixture another hr. at 0° and 0.5 h. at 20°, pouring it into 1.2 l. ice-salt-H₂O, extracting it quickly with Et₂O, and evaporating the washed (saturated NaHCO₃, H₂O) Et₂O extract in vacuo under N give 12.2 g. residue which is hydrogenated 40 min. in 25 cc. MeOH with 3 g. 5% Pd-BaSO₄, giving 83% 2-(m-methoxyphenyl)cyclohexanone (III), b_{0.02} 135-45° (air bath temperature), n_D20 1.5497. Adding (5-10 min.) 8.8 g. III in 60 cc. C₆H₆ to 1.7 g. NaNH₂ in 40 cc. refluxing C₆H₆, refluxing the solution 0.5-1 h., adding (30-45 min.) 4.8 g. CH₂ClCH₂NMe₂ in 60 cc. C₆H₆, refluxing the mixture 20 h. with stirring, washing it with H₂O, extracting it with dilute HCl, warming the acid extract slightly, washing it with Et₂O, making it basic with NH₄OH, extracting with Et₂O, and treating the dried Et₂O extract with dry HCl give 24% 2-(2-dimethylaminoethyl)-2-(m-methoxyphenyl) cyclohexanone-HCl (IV), prisms, m. 165.5-6.5°, and, from the mother liquors, 5.2 g. unchanged III. Heating 0.5 g. IV, 0.5 cc. 95% N₂H₄, 0.5 g. KOH, and 5 cc. triethylene glycol 6 h. at 180-210° and treating the reduction product with 32% HBr-AcOH give 90% 2-(2-dimethylaminoethyl)-1-(m-methoxyphenyl)cyclohexane-HBr (V), prisms, m. 167-8.5°. Refluxing 0.6 g. V 0.5 h. with 2.5 cc. 48% HBr and evaporating the solution in vacuo give 87% I.HBr, needles, m. 178-9° (HCl salt, needles, m. 191.5-3°). Treating 0.5 g. I.HBr in 0.5 cc. Ac₂O and 1 cc. C₅H₅N 1 h. at 25°, diluting the mixture with Et₂O, and keeping it overnight at 5° give 0.55 g. 1-(m-acetoxyphehyl)-1-(2-dimethylaminoethyl)cyclohexane-HBr, needles, m. 138-8.5°. Converting 12 g. IV into 12.4 g. HBr salt and treating the latter in 140 cc. refluxing AcOH with 6 g. Br in 50 cc. AcOH, diluting the mixture with 500 cc. Et₂O, and keeping it overnight at -6° give 14.5 g. 6-Br derivative-HBr of IV, needles, m. 184-5°, which, treated 1-2 h. in 35 cc. H₂O with 4 cc. concentrated NH₄OH, gives 90% 5-(m-methoxyphenyl)-2-methyl-9-oxomorphane (VI) methobromide (VII), thick plates, m. 249-50° (decomposition). Dry distillation of 10.2 g. VII at 210-25°/0.5 mm. gives 89% VI.HCl, plates, m. 203-5° (decomposition). Heating 7.7 g. VI.HCl in 50 cc. triethylene glycol with 7 cc. 95% N₂H₄ and 7 g. KOH 5.5 h. at 175° and 0.5 h. at 190° gives 90% 5-(m-methoxyphenyl)-2-methylmorphane-HBr, oblong plates, m. 165-7°, which (7.7 g.), refluxed with 30 cc. 48% HBr, gives 80% II.HBr, m. 171-2° (free base, m. 156-7.5°; m-Ac derivative-HBr, 100%, small prisms, m. 162.5-3.5°). The results of the pharmacol tests of these compds. are given in a table.

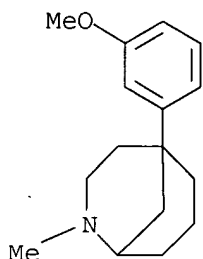
IT 27107-68-2, 2-Azabicyclo[3.3.1]nonane, 5-(m-hydroxyphenyl)-2-methyl- (and derivs.)

RN 27107-68-2 CAPLUS

CN Phenol, 3-(2-methyl-2-azabicyclo[3.3.1]non-5-yl)- (9CI) (CA INDEX NAME)



IT 53661-49-7, 2-Azabicyclo[3.3.1]nonane, 5-(m-methoxyphenyl)-2-methyl-, hydrobromide
(preparation of)
RN 53661-49-7 CAPLUS
CN 2-Azabicyclo[3.3.1]nonane, 5-(3-methoxyphenyl)-2-methyl-, hydrobromide
(9CI) (CA INDEX NAME)



● HBr

L6 ANSWER 61 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1955:28257 CAPLUS

DOCUMENT NUMBER: 49:28257

ORIGINAL REFERENCE NO.: 49:5498d-i

TITLE: Structures related to morphine. II. An isomer of N-methylmorphinan

AUTHOR(S): May, Everette L.; Murphy, James G.

CORPORATE SOURCE: Natl. Inst. of Health, Bethesda, MD

SOURCE: Journal of Organic Chemistry (1954), 19, 618-22

CODEN: JOCEAH; ISSN: 0022-3263

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB 1,2,3,9,10,10a-Hexahydro-11-methyl-1,4a(4H)-iminoethanophenanthrene (I), an isomer of N-methylmorphinan, has been synthesized from 2-(2-dimethylaminoethyl)-2-phenylcyclohexanone (II). II.HBr (0.005 mol) in 10 cc. refluxing AcOH is treated with 0.26 cc. Br in 10 cc. AcOH and the mixture refluxed 0.5 h., giving 88% 6-Br analog (III), tiny needles, m. 181-1.5°. Treating 34.6 g. III in 86 cc. H₂O with 13 cc. concentrated NH₄OH with ice-cooling gives 91% 9-keto-2-methyl-5-phenylmorphinan (IV) methobromide (V), square plates, m. 238-8.5° (IV.HCl, prepared in 88% yield by dry distillation of V at 225-30°/0.1 mm. and treating the distillate in ether with HCl, needles, crystallizing with 0.5 mol H₂O, m. 214-15°). Heating 2.2 g. IV.HCl with 0.8 cc. 95% N₂H₄, 1.6 g. KOH, and 8 cc. triethylene glycol 6 h. at 170-80°, diluting with H₂O, extracting

with

ether, and treating the ether extract with HCl give 75% 2-methyl-5-

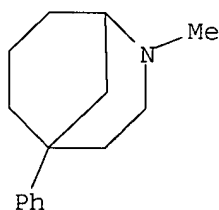
10/762,730

phenylmorphane.HCl, slender prisms, m. 239-40°. Refluxing IV (from 5.6 g. HCl salt), 1.4 g. CH₂(CN)₂, 0.4 g. NH₄OAc, 0.9 cc. AcOH, and 7 cc. C₆H₆ 1 h. with a H₂O trap, extracting with ether, and treating the ether extract with alc. HCl gives 87% 9-dicyanomethylene-2-methyl-5-phenylmorphane (VI).HCl, slim prisms, m. 210-13° (decomposition). Hydrogenating 2 g. VI.HCl in 50 cc. MeOH with 0.1 g. PtO₂ 1.5 h. at 20°, evaporating the filtered solution in vacuo, refluxing the residue 6 h. with 20 cc. 20% HCl, evaporating again, and triturating the residue with Me₂CO gives 46% 9-carbomethoxy-2-methyl-5-phenylmorphane (VII).HCl, minute prisms, m. 280° (decomposition). Heating 2.8 g. VII.HCl with 30 g. polyphosphoric acid 3 h. with stirring, diluting the mixture with ice-H₂O, pouring it into ice-H₂O containing 45 g. KOH, and extracting with ether gives 93% 1,2,3,9,10,10a-hexahydro-9-oxo-11-methyl-1,4a-(4H)-iminoethanophenanthrene (VIII).HCl, blades containing 0.5 H₂O, m. 192-4° [picrate, yellow prisms, m. 220-2° (decomposition)]. Reduction of VIII with N₂H₄ gives 84% I.HCl, needles, m. 244-5.5° (decomposition) [picrate, yellow needles, m. 192-3° (decomposition)]. Heating the methiodide (m. about 320°) of I with 0.5 g. Ag₂O and 5 cc. H₂O 45 min. on a steam bath, evaporating the filtered solution in vacuo, and dry-distilling the residue at 120-30°/0.5 mm. give 0.25 g. distillate which, hydrogenated with PtO₂ 15-20 min. and treated with picric acid, gives 35% 4a-(2-dimethylaminoethyl)-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (IX) picrate, yellow blades, m. 185-7°; it gives no m.p. depression when mixed with IX picrate obtained from n-methylmorphinan (cf. Grewe and Mondon, C.A. 43, 4279a). IX.HCl, square plates, m. 213-14°.

IT 74904-15-7, 2-Azabicyclo[3.3.1]nonane, 2-methyl-5-phenyl-, hydrochloride
(preparation of)

RN 74904-15-7 CAPLUS

CN 2-Azabicyclo[3.3.1]nonane, 2-methyl-5-phenyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

=> d his

(FILE 'HOME' ENTERED AT 15:48:53 ON 24 JAN. 2005)

FILE 'REGISTRY' ENTERED AT 15:49:09 ON 24 JAN 2005

L1 STRUCTURE UPLOADED
L2 14 S L1
L3 STRUCTURE UPLOADED
L4 13 S L3
L5 408 S L3 FULL

FILE 'CAPLUS' ENTERED AT 15:53:54 ON 24 JAN 2005

L6 61 S L5

10/762,730

=> d 13

L3 HAS NO ANSWERS

L3 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=> d 11

L1 HAS NO ANSWERS

L1 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=>



PALM INTRANET

Day : Monday
Date: 1/24/2005
Time: 16:06:50**Inventor Name Search Result**

Your Search was:

Last Name = COE

First Name = JOTHAM

Application#	Patent#	Status	Date Filed	Title	Inventor Name 51
60497372	Not Issued	159	08/22/2003	PHARMACEUTICAL COMPOSITION FOR THE PREVENTION AND TREATMENT OF ADDICTION IN A MAMMAL	COE, JOTHAM WADSWORTH
60497353	Not Issued	159	08/22/2003	PHARMACEUTICAL COMPOSITION FOR THE TREATMENT OF OBESITY OR TO FACILITATE OR PROMOTE WEIGHT LOSS	COE, JOTHAM W.
60497350	Not Issued	159	08/22/2003	PHARMACEUTICAL COMPOSITION FOR THE PREVENTION AND TREATMENT OF ADDICTION IN A MAMMAL	COE, JOTHAM WADSWORTH
60496803	Not Issued	018	08/21/2003	PHARMACEUTICAL COMPOSITION FOR THE PREVENTION AND TREATMENT OF ADDICTION IN A MAMMAL	COE, JOTHAM WADSWORTH
60488764	Not Issued	159	07/21/2003	ARYL FUSED AZAPOLYCYCLIC COMPOUNDS	COE, JOTHAM W.
60488760	Not Issued	159	07/21/2003	HETEROARYL FUSED AZAPOLYCYCLIC COMPOUNDS	COE, JOTHAM W.
60469493	Not Issued	159	05/09/2003	PHARMACEUTICAL COMPOSITION FOR THE TREATMENT OF OBESITY OR TO FACILITATE OR PROMOTE WEIGHT LOSS	COE, JOTHAM W.
60469429	Not Issued	159	05/09/2003	PHARMACEUTICAL COMPOSITION FOR THE PREVENTION AND TREATMENT OF NICOTINE	COE, JOTHAM W.

				ADDICTION IN A MAMMAL	
<u>60462651</u>	Not Issued	159	04/14/2003	4-PHENYL-PIPERIDINE COMPOUNDS AND THEIR USE AS MODULATORS OF OPIOID RECEPTORS	COE, JOTHAM W.
<u>60462629</u>	Not Issued	159	04/14/2003	3-AZABICYCLO[3.2.1]OCTANE DERIVATIVES	COE, JOTHAM W.
<u>60462605</u>	Not Issued	159	04/14/2003	2-AZABICYCLO[3.3.1]NONANE DERIVATIVES	COE, JOTHAM W.
<u>60416654</u>	Not Issued	159	10/07/2002	MODULAR UTILITIES MANIFOLD	COE, JOTHAM WADSWORTH
<u>60409694</u>	Not Issued	159	09/10/2002	DIAZABICYCLIC COMPOUNDS USEFUL IN THE TREATMENT OF CNS AND OTHER DISORDERS	COE, JOTHAM W.
<u>60303957</u>	Not Issued	159	07/09/2001	PHARMACEUTICAL COMPOSITION AND METHOD OF MODULATING CHOLINERGIC FUNCTION IN A MAMMAL	COE, JOTHAM W.
<u>60258736</u>	Not Issued	159	12/29/2000	PHARMACEUTICAL COMPOSITION FOR THE TREATMENT OF CNS AND OTHER DISORDERS	COE, JOTHAM W.
<u>60221718</u>	Not Issued	159	07/31/2000	PHARMACEUTICAL COMPOSITION FOR THE TREATMENT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD)	COE, JOTHAM W.
<u>60208856</u>	Not Issued	159	06/02/2000	PHARMACEUTICAL COMPOSITION FOR THE TREATMENT OF OBESITY OR TO FACILITATE OR PROMOTE WEIGHT LOSS	COE, JOTHAM W.
<u>60202799</u>	Not Issued	159	05/09/2000	PHARMACEUTICAL COMPOSITION AND METHOD OF TREATMENT OF DISEASES OF COGNITIVE DYSFUNCTION IN A MAMMAL	COE, JOTHAM W.
<u>60195738</u>	Not Issued	159	04/07/2000	PHARMACEUTICAL COMPOSITION FOR TREATMENT OF ACUTE, CHRONIC PAIN AND/OR NEUROPATHIC PAIN AND MIGRAINES	COE, JOTHAM W.
<u>10833714</u>	Not	092	04/27/2004	PHARMACEUTICAL	COE, JOTHAM

	Issued			COMPOSITION FOR THE TREATMENT OF CNS AND OTHER DISORDERS	WADSWORTH
<u>10824037</u>	Not Issued	020	04/14/2004	3-AZABICYCLO[3.2.1]OCTANE DERIVATIVES	COE, JOTHAM W.
<u>10823026</u>	Not Issued	020	04/13/2004	4-PHENYL-PIPERIDINE COMPOUNDS AND THEIR USE AS MODULATORS OF OPIOID RECEPTORS	COE, JOTHAM W.
<u>10793112</u>	Not Issued	030	03/04/2004	PHARMACEUTICAL COMPOSITION FOR THE PREVENTION AND TREATMENT OF NICOTINE ADDICTION IN A MAMMAL	COE, JOTHAM W.
<u>10791984</u>	Not Issued	030	03/03/2004	PHARMACEUTICAL COMPOSITION FOR THE TREATMENT OF OBESITY OR TO FACILITATE OR PROMOTE WEIGHT LOSS	COE, JOTHAM W.
<u>10783790</u>	Not Issued	030	02/20/2004	PHARMACEUTICAL COMPOSITION AND METHOD OF MODULATING CHOLINERGIC FUNCTION IN A MAMMAL	COE, JOTHAM W.
<u>10764167</u>	Not Issued	092	01/23/2004	ARYL FUSED AZAPOLYCYCLIC COMPOUNDS	COE, JOTHAM WADSWORTH
<u>10762730</u>	Not Issued	030	01/22/2004	2-AZABICYCLO[3.3.1]NONANE DERIVATIVES	COE, JOTHAM W.
<u>10762447</u>	Not Issued	020	01/22/2004	4-PHENYL-PIPERIDINE COMPOUNDS AND THEIR USE AS MODULATORS OF OPIOID RECEPTORS	COE, JOTHAM W.
<u>10681290</u>	Not Issued	020	10/06/2003	MODULAR UTILITIES MANIFOLD	COE, JOTHAM WADSWORTH
<u>10657738</u>	Not Issued	030	09/08/2003	DIAZABICYCLIC COMPOUNDS USEFUL IN THE TREATMENT OF CNS AND OTHER DISORDERS	COE, JOTHAM W.
<u>10366532</u>	Not Issued	061	02/13/2003	PHARMACEUTICAL COMPOSITION FOR THE TREATMENT OF OBESITY OR TO FACILITATE OR PROMOTE WEIGHT LOSS	COE, JOTHAM WADSWORTH
<u>10348399</u>	Not Issued	061	01/21/2003	PHARMACEUTICAL COMPOSITION FOR THE PREVENTION AND	COE, JOTHAM W.

				TREATMENT OF NICOTINE ADDICTION IN A MAMMAL	
<u>10348381</u>	Not Issued	041	01/21/2003	SYSTEM AND METHOD FOR FULL WIRELESS SYNCHRONIZATION OF A DATA PROCESSING APPARATUS WITH A MESSAGING SYSTEM	COE, JOTHAM W
<u>10347955</u>	Not Issued	161	01/21/2003	PHARMACEUTICAL COMPOSITION AND METHOD OF TREATMENT OF DISEASES OF COGNITIVE DYSFUNCTION IN A MAMMAL	COE, JOTHAM WADSWORTH
<u>10336532</u>	Not Issued	041	01/03/2003	ARYL FUSED AZAPOLYCYCLIC COMPOUNDS	COE, JOTHAM WADSWORTH
<u>10336508</u>	Not Issued	041	01/03/2003	ARYL FUSED AZAPOLYCYCLIC COMPOUNDS	COE, JOTHAM WADSWORTH
<u>10229447</u>	<u>6809094</u>	150	08/28/2002	PHARMACEUTICAL COMPOSITION FOR THE TREATMENT OF CNS AND OTHER DISORDERS	COE, JOTHAM WADSWORTH
<u>10217771</u>	<u>6706702</u>	150	08/13/2002	ARYL FUSED AZAPOLYCYCLIC COMPOUNDS	COE, JOTHAM WADSWORTH
<u>10131278</u>	Not Issued	092	04/23/2002	ARYL FUSED AZAPOLYCYCLIC COMPOUNDS	COE, JOTHAM WADSWORTH
<u>10105605</u>	Not Issued	161	03/25/2002	PHARMACEUTICAL COMPOSITION AND METHOD OF MODULATING CHOLINERGIC FUNCTION IN A MAMMAL	COE, JOTHAM W.
<u>10075843</u>	Not Issued	092	02/13/2002	ARYL FUSED AZAPOLYCYCLIC COMPOUNDS	COE, JOTHAM WADSWORTH
<u>10075348</u>	Not Issued	041	02/14/2002	ARYL FUSED AZAPOLYCYCLIC COMPOUNDS	COE, JOTHAM W.
<u>10047850</u>	Not Issued	161	10/23/2001	PHARMACEUTICAL COMPOSITION FOR THE TREATMENT OF CNS AND OTHER DISORDERS	COE, JOTHAM WADSWORTH
<u>09865793</u>	Not Issued	161	05/25/2001	PHARMACEUTICAL COMPOSITION FOR THE TREATMENT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD)	COE, JOTHAM WADSWORTH
<u>09850042</u>	Not Issued	161	05/07/2001	PHARMACEUTICAL COMPOSITION FOR THE TREATMENT OF OBESITY OR	COE, JOTHAM WADSWORTH

				TO FACILITATE OR PROMOTE WEIGHT LOSS	
09760966	Not Issued	161	01/16/2001	PHARMACEUTICAL COMPOSITION AND METHOD OF TREATMENT OF DISEASES OF COGNITIVE DYSFUNCTION IN A MAMMAL	COE, JOTHAM WADSWORTH
09740307	Not Issued	161	12/18/2000	PHARMACEUTICAL COMPOSITION FOR TREATMENT OF ACUTE, CHRONIC PAIN AND/OR NEUROPATHIC PAIN AND MIGRAINES	COE, JOTHAM W.
09697749	Not Issued	161	10/26/2000	PHARMACEUTICAL COMPOSITION FOR THE PREVENTION AND TREATMENT OF NICOTINE ADDICTION IN A MAMMAL	COE, JOTHAM W.
09582513	6462035	150	08/07/2000	ARYL FUSED AZAPOLYCYCLIC COMPOUNDS	COE, JOTHAM WADSWORTH
09578369	Not Issued	168	05/25/2000	PHARMACEUTICAL COMPOSITION FOR THE PREVENTION AND TREATMENT OF NICOTINE ADDICTION IN A MAMMAL	COE, JOTHAM W.
09514002	6605610	150	02/25/2000	ARYL FUSED AZAPOLYCYCLIC COMPOUNDS	COE, JOTHAM W.

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